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# PATHOLOGY, CLINICAL MANIFESTATIONS AND TREATMENT OF LESIONS OF THE INTERVERTEBRAL DISKS*

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LESIONS of the intervertebral disks are extremely common, but do not induce clinical manifestations in every case. If present, clinical signs and symptoms are sometimes almost indistinguishable from those caused by diseases of the viscera, joints, muscles and other parts. In many cases, therefore, it is difficult to decide whether the symptoms should be attributed to a disk lesion or to some other cause. Accordingly there is a divergence of opinion about the clinical significance and appropriate treatment of these lesions. Some surgeons ascribe many and different symptoms to certain lesions of the disk; others tend to discount the same lesions as incidental abnormalities. Such a discrepancy seems to demand a reinvestigation of the problem by means of statistical methods.

On the basis of 826 cases of disk lesions observed during the last eight years, of a control series of 200 persons without symptoms, and of another control series of 100 persons with complaints suggestive of disk lesions, an attempt has been made to ascertain whether correlations can be established between the clinical and the anatomical findings, and whether principles can be defined by which treatment may be directed.

## PATHOLOGY

The common disk lesions seem to fall into two main groups, those caused by rupture and those due to degeneration. As a result of trauma or strain, a piece of cartilage may be detached from a normal disk,[1] or the nucleus pulposus may be squeezed out of the disk center.[2, 3] The displaced material may be pressed beyond the disk margin, either through the fibers of the longitudinal ligaments — for example, backwards into the spinal canal, where it may encroach on the cord[4, 5] — or vertically, into an adjacent vertebral body, through congenital defects[6] or traumatic fissures[7] of the osseous and cartilaginous surfaces. It appears that forward and backward displacement occurs when the disk is less resistant than the bone, and that intrusion of disk material into the vertebras implies that the bone is less resistant than the disk; but the two modes of displacement may combine.

With advancing years many disks normally lose in turgor and volume and grow flat and inelastic as a result of dehydration and increase of fibers of the disk cartilage.[8] These morphologic alterations are probably signs of a change of the colloidal phase of the connective tissue. They are believed to be caused by the innumerable unnoticed injuries of daily life.[7] In some persons this wear and tear seems to cause a premature aging or degeneration, especially of those disks that are located in the most movable vertebral regions — that is, the lower cervical and lower lumbar segments.[9, 10]

In addition to this quasi-spontaneous degeneration, fibrosis and flattening may develop as a result of disk rupture and of diseases of vertebral bone. Rupture of the disk, both into the vertebral body and through the longitudinal ligaments, often sets up a reaction marked by increasing fibrosis of the disk cartilage, indistinguishable histologically from involutionary degeneration.[3, 6] Bone disease may involve the disks either directly or indirectly. Infection of the vertebral body may spread directly into them through the sievelike lamina cribrosa; although resistant against most infections,[3] a disk, once infected, deteriorates rapidly,[11] and residual disk cartilage may undergo degeneration. But even when it escapes infection, a disk adjacent to an infected vertebral body usually grows thin and fibrous in the course of several months or years (Fig. 1), although the bone infection itself may have become arrested in the meantime. Since the disk, which is normally avascular during adult life,[6] receives its nutrition from the vertebral body,[7] it is conceivable that degeneration occurs in these cases because nu-

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trition was inadequate or faulty during the period of bone infection.

It should be recalled at this point that nothing in the pathology of the disk differs from the pathology of cartilage in general. The nucleus pulposus, the

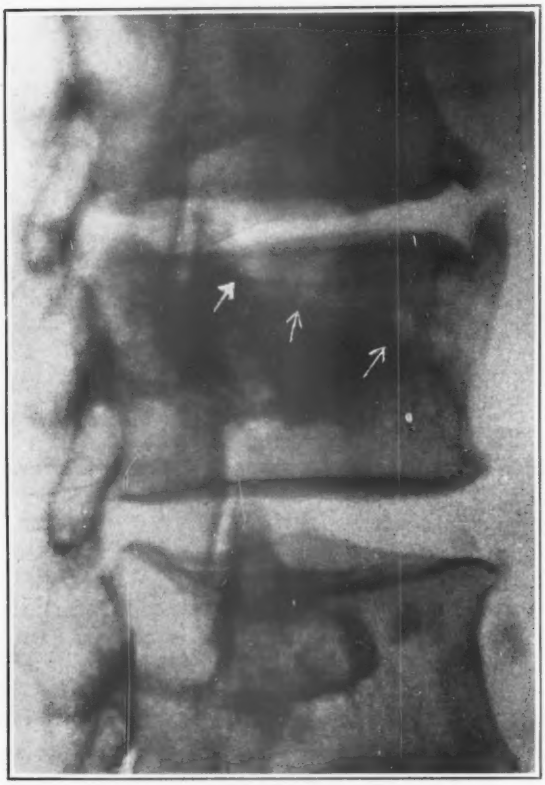

FIGURE 1. *Flattening of the Intervertebral Disk as a Result of Infection of a Vertebral Body.*

*The arrows point to small areas of rarefaction in the fourth lumbar vertebral body. The superjacent intervertebral space is about half the width of the normal subjacent interspace, owing to flattening of the disk. The patient, a forty-two-year-old man, developed sudden pain in the back during recovery from a blood-stream infection due to* Staphylococcus aureus.

presence of which somewhat complicates the picture, is an inert part that, although derived from primitive connective tissue, has no more life of its own than, for instance, the synovial fluid; it plays no active part in determining the morbid processes observed. Cartilage is a connective tissue which the omnipotent mesenchymal cell fails to regenerate effectively. It may either undergo necrosis in its various forms and phases or be invaded and replaced by vascular connective tissue. Although small scattered areas of newly formed cartilage may be produced, this repair is hardly ever sufficient to restore the original volume and resiliency of injured cartilage. Lesions of the disk exemplify this rule. The injured parts of a disk grow flat, less elastic and more fibrous, no matter what were the cause and nature of the original injury.[3] As the disk thins down, the vertebras at this level approach each other. As a result, the following changes may take place.

*Marginal osteophytes* (*hypertrophic spondylitis*). As the bufferlike action of the disk diminishes, the horizontal vertebral surfaces sustain increased statical stress and the edges of the vertebral bodies may come into contact during certain movements. This slight but continual trauma may cause minute fractures,[6] which normally[12] heal with callus formations. The fractures recur, and the callus formations grow, especially into the free space between the vertebral margin and the longitudinal ligaments,[13] thereby forming the marginal overgrowths (Fig. 2) that resemble exostoses of peripheral joints and are therefore commonly designated as osteoarthritis of the spine. According to its definition, however, osteoarthritis is a disease of the synovial joints and is marked by the wearing off of free articular cartilages. The joint formed by the disk and vertebras has no free cartilages; it is not a synovial joint but a synchondrosis, which has been named the "vertebral symphysis."[14] Hence marginal osteophytes at the level of flattened disks do not fit the anatomical definition of arthritis; and since it has been shown that they are not associated with the clinical symptoms of arthritis,[14] these osteophytes should not be grouped with arthritis.

*Osteoarthritis of the apophyseal joints* (*hypertrophic spondylarthritis*). At the level of a thinned disk the articular processes are crowded together, and their articular surfaces, or facets, become displaced, usually with the superjacent facet sliding backward and downward along the subjacent facet (Fig. 3).[15,16] This often causes straining of the surrounding capsules of the apophyseal joints and the ligaments and may produce a gradual wearing off of the articular cartilages that are affixed to the facets[12] — a lesion that corresponds in every respect to osteoarthritis of the peripheral joints and is a true arthritis of the spine. As in osteoarthritis of the peripheral joints, eburnation, ecchondroses and exostoses may, but need not, develop along the articular surfaces involved. This hypertrophic spondylarthritis occurs in less than 20 per cent of all cases of disk thinning; in the majority of cases the cartilages of the apophyseal joints seem to resist the strain successfully.[12]

*Bony impingement.* The displacement of articular processes may amount to impingement of the tip of the subjacent facet on the base of the superjacent facet.[15–17] The impinging tip may produce in the opposing base an erosion resembling a drill hole, with subsequent reactive eburnation of the surrounding bone. This was noted in 2.8 per cent of this series.

*Contact between spinous processes.* When the disk thins down, contiguous spinous processes may come into contact and form eburnation and osteophytes like the margins of the vertebral bodies.[18] This was recorded in 0.6 per cent of this series.

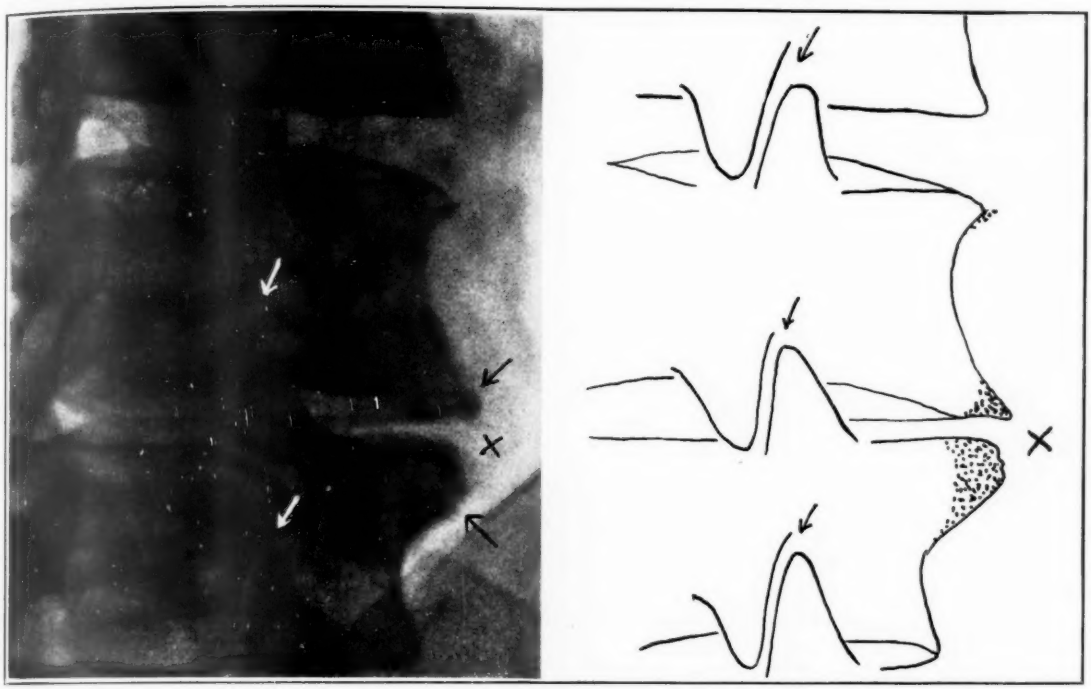

FIGURE 2. *Secondary Osteophytic Changes in the Vertebral Bone and Joints as a Result of Disk Thinning.*
*The fourth lumbar intervertebral space is less than half the width of the other interspaces, owing to flattening of its disk (x). Osteophytes have formed at the ventral margins of the vertebral bodies (black arrows), but the apophyseal joints have remained normal (white arrows). On the tracing the stippled areas correspond to the secondary lesions. The patient, a forty-one-year-old woman, complained of sciatic pain; there was no backache.*

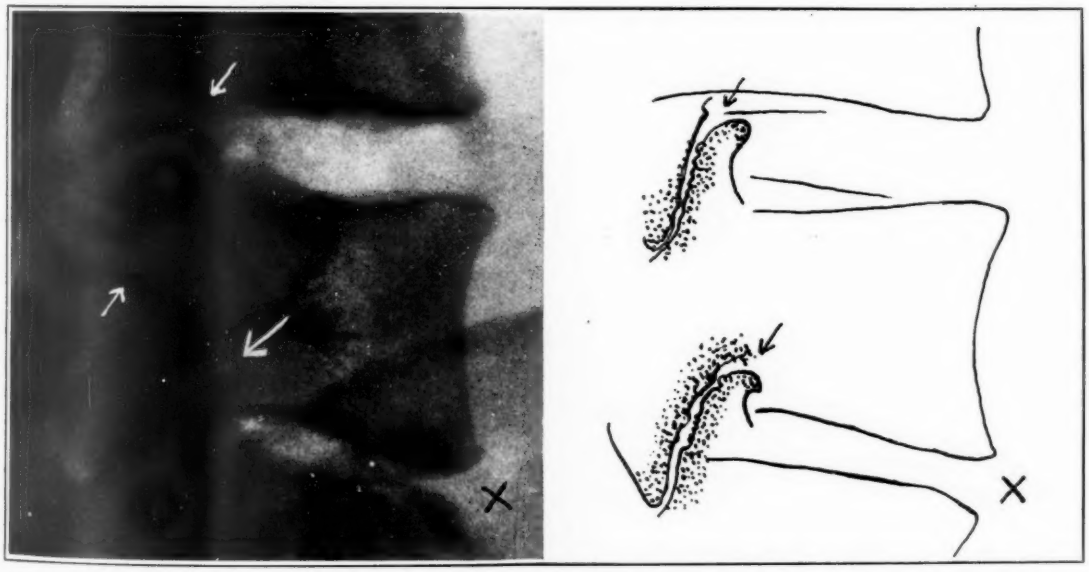

FIGURE 3. *Secondary Spondylarthritic Changes in the Vertebral Bone and Joints as a Result of Disk Thinning.*
*The fourth lumbar intervertebral disk is flattened (x). The facets at this level are ragged and eburnated, and the intervening apophyseal joint space is narrowed (white arrows). This is a diskogenetic spondylarthritis. On the tracing the stippled areas correspond to the secondary lesions. The patient, a forty-seven-year-old man, complained of severe pain in the lower back; the movements of the lumbar spine were severely restricted.*

*Narrowing of the neural foramen.* At the level of a thinned disk the neural foramen grows narrow.[13, 17, 19, 20] The nerve root that passes through it may become compressed.[16] Marginal osteophytes arising from the posterior margins of the vertebral bodies[22] and from the tips of the articular processes,[17] as well as ossification of the yellow and intra-articular ligaments[17] and swelling of the apophyseal-

joint capsule,[12] may add to the compression. The most frequent sites of pressure on nerve roots are the lower cervical and lower lumbar segments, not only because disk thinning is commonest in these regions,[9, 10] but chiefly because the nerve roots are thicker and the foramens not proportionally wider than in other vertebral sections. Since the caliber of the nerve root, the original width of the foramen and the amount of narrowing vary from case to case,[14, 23] compression of nerve roots does not occur in every case of disk thinning. Narrowing of neural foramens was present in 92 per cent of the cases of disk thinning in this series.

*Bulging of disks into the spinal canal.* A softened, fibrosed or thinned disk may, under the pressure of superincumbent parts, be flattened out so that it protrudes beyond the vertebral edges. Since the longitudinal ligaments at the level of a flattened disk grow loose,[13] they yield and bulge sideward, together with the disk. The protruding parts may cause pressure on the spinal cord.[24]

The secondary changes above enumerated have been designated as "diskogenetic," in order to imply that they are all caused by the disk lesion. One may speak of diskogenetic osteophytes, diskogenetic spondylarthritis and so forth, in order to distinguish these lesions from similar alterations that are due to some other cause. Marginal osteophytes, for instance, may be present at the level of perfectly normal disks, especially as a result of low-grade bone infection, and osteoarthritis of the apophyseal joints may be produced by several different factors.[12, 14] The clinical manifestations associated with disk lesions have been named "the diskogenetic syndrome," and the totality of anatomical and clinical findings has been termed "diskogenetic disease."[10]

## Clinical Manifestations

Not every disk lesion produces clinical manifestations. In a series of 200 apparently healthy persons not conscious of any symptoms, flattened disks were found in 22 cases (11 per cent). Conversely, in a series of 312 unselected cases of disk thinning, clinical signs and symptoms pointing to a lesion of the involved vertebral segments were present, or had been present at different periods, in 267 cases (85 per cent). These figures dovetail with a sufficient degree of accuracy, but are not necessarily representative. In many cases the symptoms are transient or recurrent rather than persistent; and when a patient happens to be free of pain and discomfort at the time of the x-ray examination, he is classified with the "silent" group, although he may develop symptoms in the future, or may have forgotten about symptoms that he had in the past. One often hears patients state that they never had any pain or disability until they are reminded by a companion of the "sciatica," "rheumatism" or "sore shoulder," for which they consulted physicians and osteopaths in previous years.[12]

The main difficulty in evaluating the clinical significance of disk lesions consists in the fact that signs and symptoms virtually identical with those caused by diseases of the disk may be the result of involvement of viscera, muscles, bursas, peripheral joints, spinal cord, and peripheral nerves. In a series of 100 patients complaining of symptoms suggestive of lesions of the cervical disks, flattening of the disks was demonstrable in 89 cases (89 per cent); in 34 of these, 11 showed evidence of bursitis, 5 of acromioclavicular arthritis, 2 of tuberculosis of the shoulder, and 17 of aortic sclerosis, coronary disease and cardiac failure. In the remaining 11 cases, myalgia, polyneuritis and subdeltoid bursitis were present in the absence of disk lesions in 8 patients, and the source of the complaint could not be ascertained in 3 cases. This shows that clinical manifestations suggestive of disk lesions are due to some other diseases in about 10 per cent of the cases, and that their connection with a demonstrable disk lesion is questionable in at least another third.

From these observations it should be inferred that the roentgenographic demonstration of a diseased disk does not prove the diskogenetic origin of the complaint. This limitation was perhaps not sufficiently emphasized in early reports, including mine.[17, 25] On the other hand, the figures indicate that in about two thirds of the cases, certain clinical manifestations are in all probability due to the disk lesions disclosed on roentgenograms.

Axiomatic notions have obscured the problem. For instance, some authors [13, 24, 26] maintain that narrowing of a neural foramen cannot amount to compression of the nerve root by the surrounding bone. Anatomic specimens showing such a compression were presented by Hadley[16] in 1938. In the same year, unquestionable clinical evidence of damage to nerve roots passing through narrowed neural foramens was submitted.[13] The signs and symptoms noted in these patients were found to reappear in those cases in which examination suggested, but did not prove beyond doubt that the clinical manifestations were actually caused by the disk lesions present. These manifestations were as follows:

*Pain in the back or neck at the level of the involved disk.* This is not common; it was noted in 21 per cent of this series; its incidence varied with the vertebral region involved.

*Limitation of vertebral movements at the level of the involved disks.* This was recorded in 18 per cent of the series and varied with the localization of the disk lesion.

*Manifestations of radicular neuralgia or neuritis.* These are multifarious, consisting of pain in the peripheral region that corresponds to the involved nerve segment, weakness and atrophy of muscles, hyperesthesia, paresthesia and anesthesia, and trophic changes of the skin,

muscle and bones. Manifestations of radicular neuralgia and neuritis were present in 72 per cent of the series.

## Correlations between Clinical and Anatomical Findings

A study of the correlations between the clinical and anatomical findings above classified seems to show that the clinical manifestations of disk lesions vary with a number of factors.

*Vertebral region involved.* Flattening of cervical disk was associated with pain in the neck in 4 per cent of the cases; with limited motion of the cervical spine in 11 per cent; and with recurrent pain in the shoulders, forearm, precordium and fingers in 72 per cent. In the presence of flattened thoracic disks pain in the back was noted in 29 per cent of the patients; limited motion of the thoracic spine could not be determined, since the movements of this region are normally very scant; and persistent or recurrent intercostal neuralgia, occasionally accompanied by recurrent herpes zoster, was present in 36 per cent of the cases. Of the patients with flattened lumbar and lumbosacral disks, 37 per cent complained of pain in the low back, 31 per cent of limited motion in this region, and 49 per cent of recurrent sciatic pain.

*Thinning of disks.* The incidence and severity of the clinical manifestations were not proportional to the degree of disk thinning, as measured by the width of the intervertebral space. No correlation could be established between any of the clinical signs and symptoms, on the one hand, and the degree of disk thinning, on the other.

*Involvement of other vertebral parts.* The presence, amount and size of osteophytes at the anterior margins of the vertebral bodies did not seem to determine the incidence, kind and severity of the clinical manifestations. All things being equal, the signs and symptoms were the same in patients with and those without osteophytes. Osteophytes at the posterior margins of the vertebral bodies seemed to accentuate and maintain radicular nerve pain; all things being equal, the incidence of radicular neuralgia was 43 per cent higher in the presence than in the absence of these exostoses.

Bony impingement of articular processes was associated with persistent backache and with limitation of vertebral motion in all the cases; no case of bony impingement without definite clinical symptoms was encountered. Radicular pain was present in 69 per cent of these patients. In 89 per cent of the patients with diskogenetic involvement of the apophyseal joints (hypertrophic spondylarthritis), pain and diminished mobility of the involved vertebral region were noted, often associated with tenderness on pressure (Fig. 4). Conversely, only 8 per cent of all patients with thinned disks but without involvement of the apophyseal joints were conscious of pain, discomfort or stiffness of the involved parts of the spine (Fig. 5). Contact between spinous processes did not seem to alter or accentuate the symptoms present and was noted in an equal number of patients who were free of symptoms. The cases of bulging of a degenerated disk into the spinal canal were not numerous enough to warrant statistical evaluation.

These observations indicate that the clinical manifestations of disk lesions are determined, at least to some extent, by two main factors: the vertebral region involved, and the condition of the apophyseal joints. Lesions of cervical disks rarely cause any symptoms in the neck itself, but lesions of the lumbar and lumbosacral disks cause low-back pain and limitations of movements in about one third of the cases. On the other hand, lesions of cervical disks induce radicular manifestations in a majority of cases, and lesions of the lumbar and lumbosacral disks cause radicular neuralgia in only about one half of the cases. Lesions of the thoracic disks seem to remain clinically silent in about two thirds of the patients. Pain and limited motion in the spine seem to develop chiefly when the apophyseal joints have become involved, irrespective of the seat of the lesion.

On the negative side stand two findings that, although conspicuous, do not seem to play a part in determining the clinical manifestations in most cases. These are osteophytes of the vertebral margins — so-called "osteo-arthritis of the spine" — and the amount of disk thinning. Marginal osteophytes, no matter how large and numerous, do not cause symptoms unless they arise at the posterior vertebral edges and project into the neural foramens. These posterior osteophytes occur not infrequently in the cervical spine,[13, 17, 22, 23] but are rare in the lumbar region and usually absent in the thoracic vertebras; they are difficult to recognize on routine radiograms and are usually overlooked. The only influence that osteophytes of the anterior vertebral edges seem to have, according to my observations, is that they may limit anterior flexion of the spine when they are bulky; but the patients are rarely conscious of this limitation, even when it can be definitely shown on roentgenograms made during movements of the spine. Finally, the amount of disk thinning did not seem to be responsible for the incidence and severity of clinical manifestations in this series. In many patients who were free of symptoms complete obliteration of the intervertebral spaces was present, whereas in others severe radicular neuralgia seemed to be caused by only moderate thinning of disks.

These observations confirm the contention previously made — namely, that lesions of the disks cause symptoms felt in the periphery rather than in the spine, and that, in the presence of disease of the spine, pain and rigidity of vertebral regions are caused in most cases by involvement of the apophys-

eal joints. Since disk lesions induce arthritis of the apophyseal joints in only about one fifth of the cases, symptoms felt in the spine are not common, and the vertebral origin of peripheral pain easily escapes recognition.

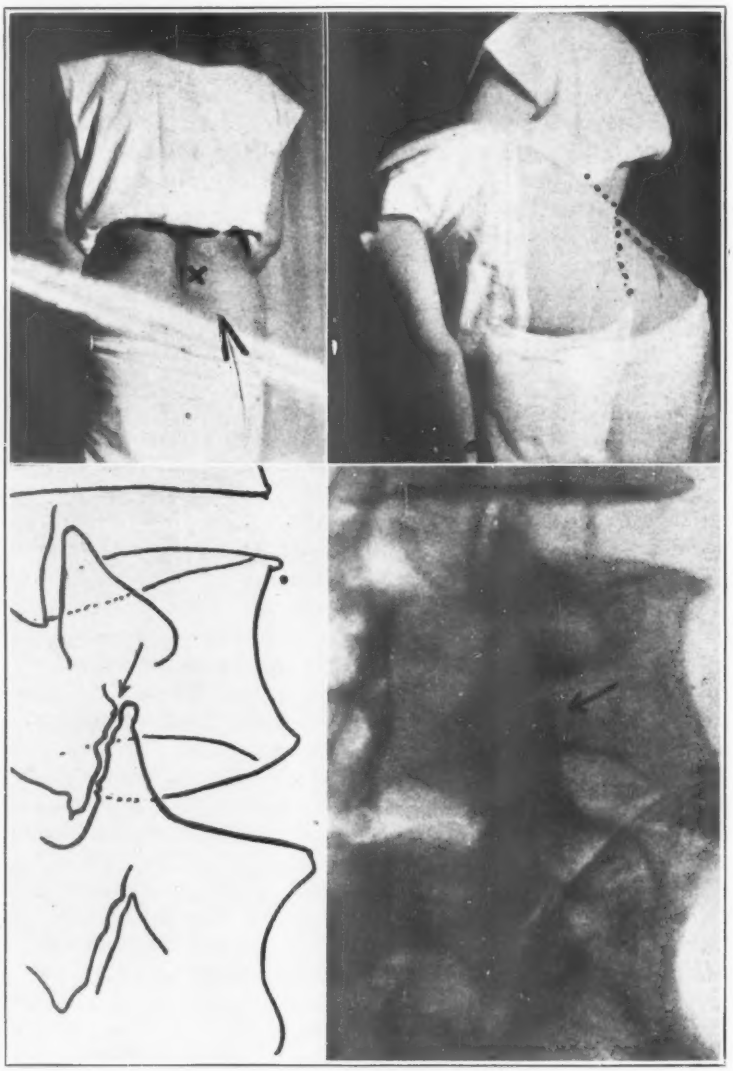

FIGURE 4. *Result of Disk Thinning with Involvement of Apophyseal Joints. The fourth lumbar interspace is narrowed, and the apophyseal joint at this level has ragged facets and a narrowed articular space (arrow, right lower corner). Compare with normal superjacent apophyseal joint. The patient, a thirty-six-year-old woman, had severe persistent pain in the back, with tenderness on pressure (x, left upper corner), impaired forward flexion (right upper corner) and no sciatic pain.*

## CLINICAL COURSE OF DISKOGENETIC DISEASE

On the basis of the data above reported, and taking into account the experience with other patients not included in this series, one may draw a composite picture of the usual course of diskogenetic disease.

*Early stage.* Rarely before the age of thirty, and usually after the age of forty-five, recurrent pain said to resemble toothache in the shoulder, wrist or gluteal region or in sciatic distribution is the commonest complaint for which medical advice is sought by these patients. The pain tends to be severer in the early morning, when it may awaken the patients, and subsides in the course of the day, to reappear in the evening. There is rarely pain in the back or neck at this stage, but a sensation of moderate stiffness may be present; it is often compared by patients to the muscle soreness that follows unwonted exercise. The symptoms may subside gradually without treatment in the course of about two years and need not recur. A history of a trauma incurred many years previously, such as a fall from

a horse, a diving accident and so forth, is obtained in many cases.

*Moderately advanced stage.* The pain in the extremities, shoulder and gluteal region becomes more pronounced, and the intervals of relative or complete relief grow shorter. The movements of the painful shoulder or leg are definitely limited, apparently as a result of muscular defense. Sensory disturbances, such as numbness and tingling of the fingertips and of the soles, set in, and so-called "electric" sensations in the arm or leg may wake the patients with a sudden shock at night. The grip of the hand may become weak, and the involved leg feels heavy. Usually some degree of atrophy of the deltoid, biceps, interosseous and thenar muscles, or of the corresponding muscles of the leg, is noted. Spontaneous recovery at this stage seems to be exceptional.

*Advanced stage.* As the disease progresses, the pain becomes persistent and muscular atrophy becomes definite. Pain in the low back and neck may be superadded. The movements of the involved limb are definitely limited owing to weakness of the muscles. Carving meat, fastening a dress on the back, tipping the hat and lifting an object from the floor are some of the movements that cannot be carried out. Trophic changes, such as herpes zoster (Fig. 6), may occur. Atrophy of the skin, especially in the region proximal to the nails, may develop, and the phalangeal bones may become rarefied.[23] In many cases the reaction of degeneration is positive. Finally a peculiar resilient swelling of the wrist, fingers or foot may develop, and the involved limb becomes completely disabled (Fig. 7). At this stage, spontaneous improvement does not occur, and the hand or foot becomes crippled if not treated.

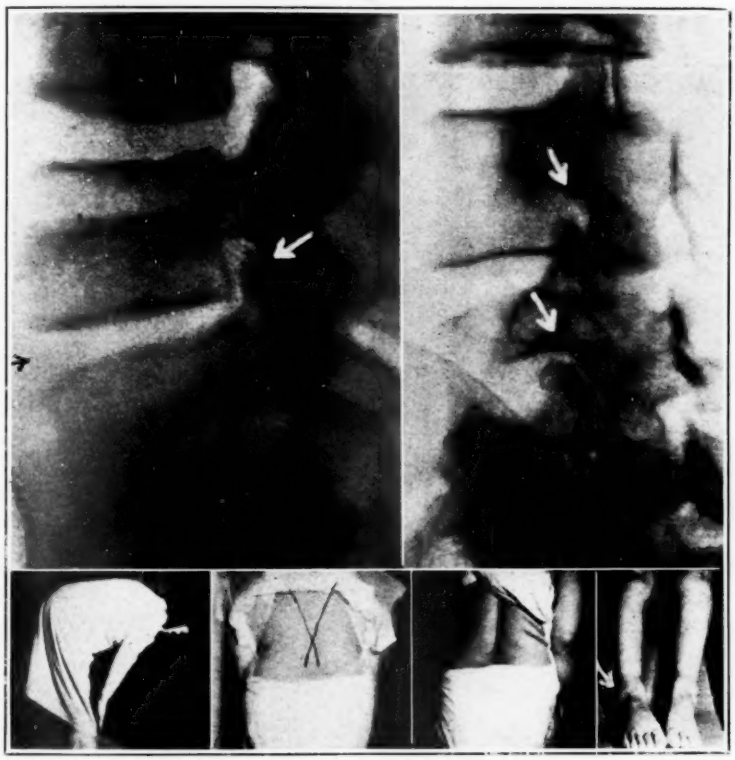

FIGURE 5. *Result of Disk Thinning without Involvement of Apophyseal Joints. The fourth lumbar interspace is narrowed (arrows, left upper corner), but the apophyseal joints at this level are normal (white arrows, right upper corner). This patient had severe sciatica with trophic edema of the right foot (arrow, right lower corner), with perfect mobility of the lumbar spine.*

Secondary deviations of the bones produce an appearance suggesting a severe deforming arthritis, but the joints are not involved and passive mobility is preserved. From these manifestations the symptoms of rupture of the disk into the spinal canal differ in the acute onset and persistence, but not in kind and severity. Such signs as back pain induced by sneezing and coughing are certainly not typical of disk rupture, and may be observed in the presence of various other lesions of the vertebras.

## CONTRIBUTING FACTORS

In this series there were as many men as women patients with symptoms referable to disk lesions.

The highest incidence of diskogenetic symptoms in women was found in the age group of sixty to seventy years, but in men in the fifty-to-sixty-year group. Weight, height and general build did not seem to play significant parts. There were short, tall, stocky and slender people with the same symptoms, but symptoms seemed to appear at a younger age in stocky than in slender patients. Occupational and social factors could not be ascertained as contributing causes.

In 74 per cent of the patients, the diskogenetic symptoms were preceded by an infection, such as sore throat, sinusitis or cystopyelitis, and the complaint persisted after the infection had subsided. One may speculate whether this can be explained on the basis of a disturbed vitamin B metabolism. It is known that in the presence of most infections the vitamin B reserve is diminished, especially in the liver. It is conceivable that this deficiency affects first or foremost those nerve segments that have already sustained some damage as a result of compression in narrowed neural foramens. If infection alone were responsible for neuralgia in these cases, one would expect other nerve segments also to become involved. One may perhaps say that a localized nerve injury that was clinically silent previous to the infection becomes manifest as a result of infection, and that infection precipitates the appearance of clinical symptoms. The influence of mental factors is difficult to determine.

## Treatment

Reasonably complete follow-up records are available in 322 cases. The patients treated were observed during periods varying between eight months and seven years. Most of them were examined at intervals of eight to ten months.

An injured disk cannot be repaired; the fibrous tissue produced cannot be reversed into cartilage. Most of the clinical manifestations, however, are caused not by the disk lesion itself but by the secondary alterations in the neural foramens and apophyseal joints resulting from the constriction of the intervertebral space. Rupture of the disk into the spinal canal is not always an exception to this rule; as will be shown, some of the symptoms associated with disk rupture may be caused by the associated disk thinning. If the narrowed intervertebral space could be rewidened permanently, no other treatment would perhaps be necessary, but this has not yet been achieved. Spinal fusion and grafting does not help to hold the vertebras permanently at

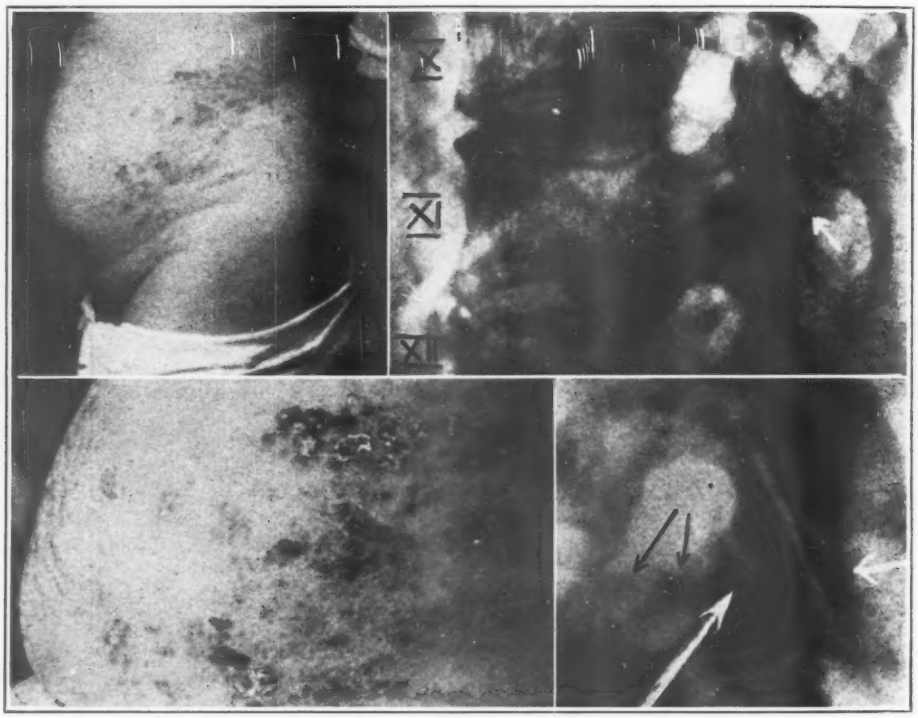


Figure 6. *Persistent Herpes Zoster as a Result of Diskogenetic Narrowing of Neural Foramens with Radicular Neuritis.*

*The neural foramen between the eleventh and twelfth thoracic vertebras is narrowed, and arthritic deformities encroach upon it (black arrows, right lower corner). There was a herpes zoster in the corresponding skin areas, persisting for a period of seven years. The pictures of the lower row were taken twenty-one months after those of the upper row. The patient was a sixty-three-year-old man.*

normal distance, since in the course of a few years the fused or grafted osseous parts yield to the stress exerted by superincumbent parts. Treatment, therefore, still remains confined to attempts at controlling and eliminating pressure on the cord, radicular neuritis and manifestations of spondylarthritis. Although from the academic point of view this does not appear to be satisfactory, it often brings about considerable relief from, and sometimes complete disappearance of, pain and disability in this group of patients.

The surgical treatment of rupture of the disk into the spinal canal has been exhaustively discussed in the literature.[5, 9, 27, 28] The scientific achievement and practical value of this procedure are uncontested, but there seems to be no complete agreement on the indications for operation. On the one hand, the fact that a patient consults a doctor because of persistent backache and sciatic pain has been considered a sufficiently valid reason for operation; on the other hand, it has been repeatedly shown that numerous lesions may produce the same clinical manifestations and roentgenographic appearance as does a ruptured disk.[29]

Of 10 patients operated on by leading surgeons five years ago and earlier, 4 are still free of symptoms, but the clinical manifestations recurred in 6 patients, of whom 2 are now almost completely incapacitated. The failures in this series were due to two main causes. In 2 cases the symptoms were not caused by the rupture alone, but in part by the associated compression of nerve roots in the neural foramens and the displacement of the facets. Although compression of the cord was relieved by the operation, pressure on the roots in the foramens seemed to persist. In the 4 other cases the involved intervertebral space grew progressively narrow in the course of three or four years in spite of spinal fusion, probably because the ruptured disk degenerated and became flat, as set forth above. The recurrence of symptoms was probably produced by compression of nerve roots within the foramens.

In spite of these observations, the definite value of surgery should not be minimized, but perhaps sufficient time has not yet elapsed to judge on the long-range results of this operation.

Conservative treatment[30, 31] consists in attempts at preventing further damage to the disks, in eliminating contributing factors and in control of pain.

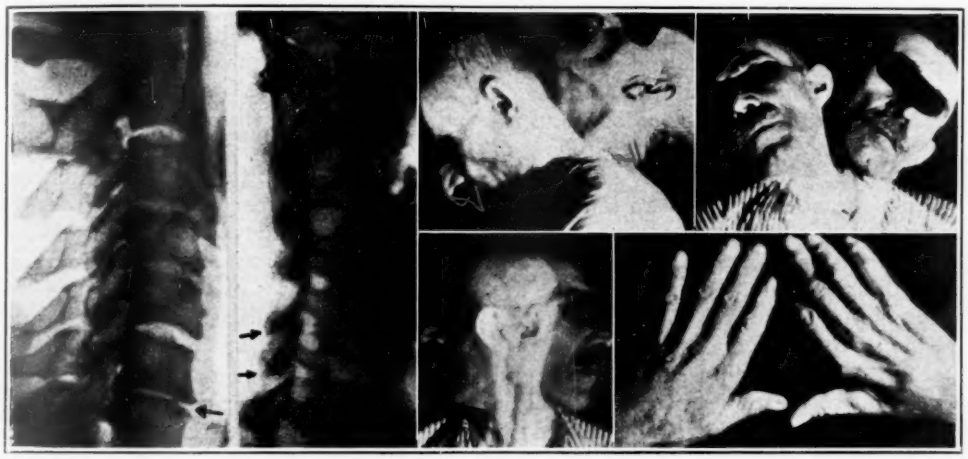

FIGURE 7. *Atrophy and Deformity of the Right Hand as a Result of Diskogenetic Radicular Neuritis. The disks below the fourth and sixth cervical vertebral bodies are flat, and the neural foramens at these levels are narrowed (arrows). The interosseous muscles of the right hand are severely atrophic, and the fingers are claw-like. Mobility of neck was perfect. The patient, a fifty-eight-year-old man had had recurrent pain in the right shoulder for about six years. One year previous to examination, the right hand became swollen and very painful. The swelling subsided, but the hand remained disabled. He had never had any pain or stiffness of the neck. The case illustrates the peripheral localization of diskogenetic manifestations.*

Jarring of the spine can be prevented to some extent by wearing rubber heels and soles, refraining from lifting heavy objects and bending at the hip and knee joints instead of stooping when reaching for an object on the floor. Infections should be brought under control, and suspected dietary deficiencies should be corrected. In some cases control of pain can be achieved by these measures alone; in others the occasional use of analgesics is required, and in a third group it is necessary to teach the patients how to avoid assuming a lordotic position. During rest, the legs should be bent at the hip and knee joints, and a thick hard pillow should be placed under the neck, in order to prevent the cervical and lumbar regions from assuming a lordotic position at night. Lordosis increases an existing constriction of the neural foramens,[30] as well as an associated displacement of the articular processes. Gentle active and passive bending, recommended as a limbering-up exercise during the morning, often helps patients to overcome the pain and discomfort experienced especially at this time of the day.

The use of back braces is rarely beneficial, probably because most of these appliances hold the spine in a position of lordosis. In fact, several of the patients in this series experienced material relief as soon as these braces were removed. Various modes of traction, used in the past and recommended by various authors, including myself, have not proved to be satisfactory in recent years and have been discontinued by me and my associates.

In 582 cases reoentgen-ray therapy was used for the control of backache and of radicular nerve pain. The value of this mode of treatment is not generally recognized, and many authors believe that its effects are highly questionable. It is true that almost nothing is known about the mechanisms that underlie the results of small doses of radiation. Moreover, the application demands experience and requires the kind of personal supervision that the overburdened radiologist can ill afford to give. The doses and intervals have to be adapted to the case, the phase of the disease and sundry other factors. Hence the treatment cannot be standardized. In institutions where the pressure of more important work makes this personal supervision unfeasible, the results have been generally disappointing. Radiologists who are in the fortunate position to devote some time to this method find the results are worth the effort.

Using a technic previously reported,[14] it was found that in 74 per cent of the patients the therapeutic effects were due to the radiation itself, but not to the associated psychologic factors. Permanent relief from pain and discomfort was obtained in 21 per cent of the cases, temporary relief in 55 per cent, and doubtful or negative results in the remaining 24 per cent. In patients in whom only temporary relief was achieved, repetition of roentgen-ray therapy proved to be effective in controlling recurrences. Treatment was given with 140 to 160 kilovolts, and 5 to 20 milliamperes, with 0.5 mm. copper and 1.0 mm. aluminum filtration, through portals 15 cm. square, the single doses measured on the skin being between 35 and 75r according to the duration of symptoms, with total skin doses of between 200 and 700r per series.

Among the patients who did not respond to the various measures above summarized, the majority had well-marked arthritic changes in the apophyseal joints at or above the level of the involved disks; some others presented bony impingement of the corresponding articular processes. In the latter group, subsequent treatment with body casts, traction and eventual spinal fusion did not prove to be satisfactory.

The best results of roentgen-ray therapy were noted in patients with trophic disturbances of the skin, muscles and bones in the peripheral segments corresponding to the involved disk. With striking uniformity these severe lesions disappeared within a number of weeks after the institution of roentgen-ray irradiation, and the disabled limbs resumed normal function soon afterward. There seems to be no other mode of treatment by which these lesions can be arrested.

## Conclusions and Summary

Disk lesions are about twice as common as is duodenal ulcer. This high incidence may be explained by the evolutionary development of the human spine. The vertebral column of man does not differ essentially from that of many quadrupeds; it is closely similar to that of the cow.[32] This means that a system of bones and joints that was originally adapted to bear almost no vertical stress sustains in man the whole impact of the upright posture and locomotion. In some persons the vertebral bone is less resistant to strain than are the disks, but in a majority of adults the disk cartilages are the weakest parts of the spine. Wear and tear cause numerous minimal injuries from which the disk rarely recovers completely, since its cartilage cannot be effectively regenerated. Cartilage undergoes degeneration, with increase of fibrous tissue. The result is loss of turgor and volume of the disk. The same changes may be caused by a single severe injury and by certain diseases of the adjacent vertebral bodies from which the disk receives its nutrition. Disk rupture is one of the injuries which may be followed by degeneration. No matter what is the cause of the injury and degeneration, flattening of disks leads to narrowing of the corresponding intervertebral spaces, associated with displacement of articular processes, narrowing of the neural foramen and abnormal contact between vertebral bodies.

The clinical manifestations depend on these secondary alterations rather than on the degree of disk thinning. Narrowing of the neural foramen may cause radicular neuritis if the corresponding nerve root is compressed, but compression does not occur in every case because of the variable relations between the caliber of the nerve and the degree of constriction. Pain in the back and limitation of vertebral movements are less frequent and seem to be caused predominantly by diskogenetic involvement of the apophyseal joints.

The conspicuous predominance of symptoms experienced in radicular distribution in the periphery over symptoms felt in the spine itself is perhaps due to the fact that the disk, being devoid of nerves,[10] does not hurt when diseased. The most sensitive parts in its neighborhood are the nerve roots and the apophyseal joints. Arthritis of these joints develops in about 20 per cent of the cases of disk lesions and produces pain in the back with limitation of vertebral motion. In the majority of cases, however, the apophyseal joints remain intact, and symptoms of nerve-root compression develop without pain and rigidity of the spinal region involved. This means that in most cases lesions of disks cause symptoms felt in the limbs without symptoms felt in the back or neck.

The signs and symptoms of radicular neuralgia and neuritis are often indistinguishable from those of myalgia, peripheral arthritis, bursitis and pain referred from diseased viscera. Moreover, in the age group in which the incidence of disk lesions is highest, involvement of joints, bursas and viscera is also common. The difficulties encountered in recognizing disk lesions are chiefly caused by these diagnostic limitations. When disk lesions coexist with other diseases that are known to induce peripheral pain, the differential diagnosis can be made only after exhaustive clinical studies are made.

Treatment may be surgical or conservative. Surgical removal of a ruptured disk followed by spinal fusion does not always prevent symptoms caused by subsequent disk thinning from developing after several years. Conservative treatment yields satisfactory results in about 75 per cent of the cases.

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# PARENTERALLY ADMINISTERED AMINO ACIDS AS A SOURCE OF PROTEIN IN MAN*

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RECENT experiments have shown that the ten amino acids believed to be essential for the growth of rats[1] and for the formation of plasma proteins in dogs[2] are capable on intravenous or subcutaneous administration of replacing all or nearly all the dietary protein required by man for nitrogen equilibrium or retention and that the parenteral administration of these amino acids, supplemented with glycine, is very well tolerated by man, as it is by the dog. Aside from their fundamental interest, these observations appear to point to a valuable means of restoring body protein or protecting against its depletion in the diseased or injured person. Protein depletion is a serious complication that because of its insidious development frequently goes unrecognized until it reaches an advanced state. Among the hazards to which it predisposes may be mentioned lowered resistance to infection,[3, 4] lowered resistance to intoxication[5–7] and impaired healing of wounds.[8–10] In many forms of illness or injury the dietary intake of protein is reduced or at best normal, whereas the need for it is usually increased.[11, 12] Reduced appetite or impaired capacity for ingesting, retaining or absorbing protein may be responsible for the inadequate intake of protein.

Search for solutions acceptable to the body and capable of providing the nitrogen requirements on parenteral administration has been pursued of late and reviewed recently, and a fairly comprehensive bibliography has been compiled.[13] The readiness with which the dog utilizes solutions of pure amino acids such as those listed in Table 1 contrasts with its lower tolerance for all other protein digests,[2, 14–16] and prompted the clinical observations now in progress. The entire investigation will be reported later, but the initial observations are of sufficient interest to be recorded now. There follows the report of the case that formed the basis of this experiment.

## Case Report

The patient was a 63-year-old farmer who had developed a gastrojejunocolic fistula. Twenty-three years previously a gastroenterostomy had been performed for relief of pyloric obstruction and a perforating pyloric ulcer. He remained free from gastrointestinal complaints until a year previously, when he began to have diarrhea and lost weight. The fistula was discovered by x-ray and a colostomy was done proximal to it. Most of the lost weight was regained, but after ten months the fistula was still open. Operation was performed for excision of the fistula and closure of an apparently nonfunctioning gastroenterostomy. The colostomy remained patent. Subsequently the patient did poorly. Abdominal discomfort, nausea and vomiting were associated with an inadequate intake of food and a marked decline in weight. After 4 weeks had elapsed, the colostomy was closed successfully, and because of the poor nutritional state and the possibility that parenteral feeding would be beneficial, the patient was transferred to the Metabolic Unit.

A careful and complete record of the respective weight or volume of the food or fluid received was kept throughout the investigation. All urine, feces, vomitus and gastric washings were saved and analyzed for total nitrogen by the macro-Kjeldahl procedure. The urine was also analyzed for its content of urea and ammonia nitrogen, by the method of Van Slyke and Kugel.[17] The nitrogen content of the food was calculated from data published in standard tables of reference (Rose) and in a few instances from data furnished by the commercial processor of the food. The weight was obtained at frequent intervals and under as nearly uniform conditions as possible.

The composition of the amino acid‖ mixtures is given in Table 1. Each mixture was stirred into distilled water just below the boiling point. Filtration through hard paper was followed by autoclaving for 15 minutes at 15 pounds' pressure. The final volume of the solutions varied from 1250 to 1550 cc. and the reaction was approximately pH 5. The solutions were water clear and had a faint yellowish tinge after autoclaving.

Table 1. *Composition of Amino Acid Mixtures.*

| Amino Acid | Mixture Vh | Mixture Vn | Mixture Vx |
|---|---|---|---|
| | gm. | gm. | gm. |
| *dl*-threonine | 7 | 7 | 7.4 |
| *dl*-valine | 8 | 8 | 11.1 |
| *dl*-leucine | 15 | 15 | 22.3 |
| *dl*-isoleucine | 7 | 7 | 10.4 |
| *l*(+)-lysine hydrochloride | 15 | 15 | 11.1 |
| *l*(−)-tryptophane | 2 | 2 | 3.7 |
| *dl*-phenylalanine | 5 | 10 | 11.1 |
| *dl*-methionine | 6 | 6 | 5.9 |
| *l*(+)-histidine hydrochloride | 3 | 3 | 3.7 |
| *l*(+)-arginine hydrochloride | 5 | 5 | 5.9 |
| Glycine | 27 | 25 | 7.4 |
| Totals | 100 | 103 | 100.0 |

Administration of the amino acid solutions was simple and rapid. The day's quota was divided into two equal injections, except for the first two days of Period 2 (Table 2), when the 50 per cent larger intake was given in three equal injections. Usually the morning dose was given subcutaneously, and the afternoon dose intravenously. Intravenous injections (50 gm.) were given on the average within 60 minutes and as rapidly as within 40 minutes (3.8 mg. of nitrogen per minute per kilogram of body weight). Subcutaneous injections were given on the average within 130 minutes and as rapidly as within 70 minutes (2.2 mg. of nitrogen per minute per kilogram of body weight).

Tolerance for the amino acid solutions was high. Its limits were not reached during this experiment, although the rates of injection used were more rapid than any recorded for protein-digest solutions with freedom from clinical disturbance. No rise in body temperature as a result of the injection was observed. In fact, during periods 5 to 10 (Table 2), the temperature did not rise above 98.6°F. On two occasions thrombosis of a forearm vein followed injections, more apparently as a result of inept venipuncture than of irritation from the solution. The lower pH of the solutions as compared with that of blood appeared to afford no intolerance. The plasma chlorides and the carbon dioxide combining power of the blood remained normal throughout the period of ob-

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‖The amino acids used in this study were kindly supplied by Merck and Company, Incorporated, New York City.

servation with suitable administration of sodium and chloride. Similar high tolerance for these solutions has been found in dogs.[2,16] In these animals the upper limits of tolerance without clinical disturbance are not reached by injections as rapid as 10 mg. of nitrogen per minute per kilogram of body weight, at which rate an adequate daily protein requirement is given within 15 minutes.[16]

The first 20 days (Periods 1 to 4) were characterized by severe pyloric obstruction, and the amount of food that passed into the duodenum was small. Although the nitrogen intake of the first 5 days (Period 1) was adequate, on account of the amino acid injections (Mixture Vh), the calories from other sources were minimal and the loss of nitrogen amounted to about 3 gm. daily. During Periods 2 and 3 the patient continued to receive injections of amino acids (Mixture Vh and Mixtures Vh and Vn, respectively) and the caloric intake was increased by the daily intravenous infusion of 2000 cc. of 10 per cent glucose. This, together with small oral feedings of carbohydrate and fat, brought the daily caloric intake from all sources to an average of about 1500 calories. Nitrogen equilibrium was achieved in both periods. In Period 4, parenteral feedings were discontinued, with the result that the patient was able to eat and retain only the inadequate amount of nitrogen and number of calories listed in Table 2. At least 10.7 gm. of nitrogen was lost during this period.

The patient was returned to the Surgical Service at the end of Period 4 because further radiologic studies suggested increasing pyloric obstruction and the possibility of a penetrating peptic ulcer. Nine days following the close of the period, a subtotal gastrectomy was performed, with excision of a penetrating pyloric ulcer. After several transfusions and a cautious dietary regime the metabolic study was resumed on the 10th postoperative day (Period 5). A good positive nitrogen balance was obtained on a soft diet containing about 70 gm. of protein and 2000 calories a day.

The parenteral administration of Mixture Vn was resumed in Period 6, together with oral feedings of a diet consisting chiefly of carbohydrate and fat. More than 80 per cent of the nitrogen intake was from amino acids, and there was a satisfactory retention of nitrogen. The loss of weight noted in Periods 5 and 6, when nitrogen was being retained, appears to have been associated with discontinuance of the vigorous postoperative infusion of saline solutions, and suggests that this form of therapy may have been the cause of subclinical edema.

TABLE 2. *Summary of Data.*

| PERIOD | DAY | NITROGEN BALANCE: INTAKE | | OUTPUT IN URINE | | | BALANCE* | CALORIC INTAKE† | WEIGHT |
|---|---|---|---|---|---|---|---|---|---|
| | | Amino Acids | Food | Total Nitrogen | Urea and Ammonia Nitrogen | Undetermined | | | |
| | | *gm.* | *gm.* | *gm.* | *%* | *gm.* | *gm.* | *cal./day* | *kg.* |
| 1 | 1 | 14.7 | | 13.8 | 78 | 3.1 | | 510 | 44.12 |
| | 2 | 14.7 | | 17.5 | 78 | 3.9 | | — | |
| | 3 | 14.7 | | 19.8 | 78 | 4.4 | | 440 | 44.12 |
| | 4 | 14.7 | | 17.7 | 75 | 4.5 | | 270 | |
| | 5 | 14.7 | 0.5 | 17.7 | 79 | 3.8 | −15.8 | 970 | |
| 2 | 6 | 22.1 | | 20.6 | 70 | 6.1 | | 800 | 44.30 |
| | 7 | 22.1 | | 21.8 | 72 | 6.1 | | 800 | |
| | 8 | 14.7 | | 14.9 | 73 | 4.1 | | 1140 | |
| | 9 | 14.7 | | 16.2 | 73 | 4.4 | | 1180 | |
| | 10 | 14.7 | 5.4 | 14.6 | 72 | 4.1 | +3.7‡ | 1660 | 45.96 |
| 3 | 11 | 14.7 | | 15.7 | 75 | 3.9 | | 1390 | |
| | 12 | 14.8 | | 15.5 | 65 | 5.4 | | 1240 | |
| | 13 | 14.8 | | 15.4 | 72 | 4.4 | | 1390 | |
| | 14 | 14.8 | | 14.6 | 73 | 4.0 | | 880 | |
| | 15 | 14.8 | 7.2 | 15.7 | 74 | 4.1 | +1.6 | 660 | 44.16 |
| 4 | 16 | — | 6.6 | 10.5 | 86 | 1.5 | | 970 | |
| | 17 | — | 5.3 | 5.1 | 82 | 0.9 | | 780 | |
| | 18 | — | 4.2 | 6.4 | 84 | 1.0 | | 570 | |
| | 19 | — | 7.4 | 5.0 | 82 | 0.9 | | 950 | |
| | 20 | — | 3.7 | 6.3 | 86 | 0.9 | −10.7 | 470 | 43.50 |
| | | Interval of 18 days, with subtotal gastrectomy on the 9th day | | | | | | | |
| 5 | 21 | — | 10.3 | 5.0 | 72 | 1.4 | | 1820 | 44.17 |
| | 22 | — | 11.4 | 5.9 | 78 | 1.3 | | 1970 | |
| | 23 | — | 11.4 | 6.6 | 83 | 1.1 | +11.1 | 1970 | 42.60 |
| 6 | 24 | 14.6 | 2.4 | 10.8 | 70 | 3.2 | | 1560 | |
| | 25 | 14.4 | 2.4 | 14.6 | 73 | 4.0 | | 1630 | |
| | 26 | 14.5 | 2.6 | 14.5 | 72 | 4.0 | | 1920 | 41.29 |
| | 27 | 14.7 | 2.7 | 13.7 | 69 | 4.2 | | 1880 | |
| | 28 | 14.7 | 3.6 | 14.4 | 73 | 3.9 | +11.2 | 2510 | 41.59 |
| 7 | 29 | 13.1 | 3.6 | 12.6 | 70 | 3.8 | | 3010 | |
| | 30 | 12.6 | 3.6 | 11.3 | 66 | 3.8 | | 2770 | 42.30 |
| | 31 | 13.1 | 3.4 | 9.7 | 65 | 3.4 | | 3000 | 42.53 |
| | 32 | 12.7 | 3.4 | 9.8 | 66 | 3.3 | | 3000 | 43.06 |
| | 33 | 12.9 | 3.4 | 10.5 | 66 | 3.6 | +20.6 | 3000 | 43.34 |
| 8 | 34 | 13.1 | 3.1 | 11.9 | 66 | 4.0 | | 2740 | 43.02 |
| | 35 | 13.1 | 3.4 | 12.1 | 68 | 3.9 | | 3000 | 43.50 |
| | 36 | 13.1 | 3.4 | 11.6 | 66 | 3.9 | | 3000 | |
| | 37 | 13.1 | 3.4 | 11.9 | 66 | 4.0 | | 3000 | 43.80 |
| | 38 | 13.1 | 3.4 | 11.9 | 65 | 4.2 | +15.1 | 2920 | 43.89 |
| 9 | 39 | — | 16.0 | 8.3 | 77 | 1.9 | | 3150 | 44.70 |
| | 40 | — | 16.0 | 7.6 | 83 | 1.3 | | 3150 | 45.61 |
| | 41 | — | 16.0 | 10.2 | 85 | 1.5 | | 3150 | 45.52 |
| | 42 | — | 16.0 | 9.6 | 84 | 1.5 | | 3150 | 45.61 |
| | 43 | — | 16.0 | 8.6 | 84 | 1.4 | +28.2 | 3150 | 45.89 |
| 10 | 44 | — | 16.0 | 8.9 | 83 | 1.5 | | 3150 | 46.67 |
| | 45 | — | 16.0 | 8.1 | 82 | 1.5 | | 3150 | 46.53 |
| | 46 | — | 16.0 | 7.9 | 84 | 1.3 | | 3150 | 46.77 |
| | 47 | — | 16.0 | 8.7 | 85 | 1.3 | | 3150 | 47.14 |
| | 48 | — | 16.0 | 9.3 | 85 | 1.4 | +28.6 | 3150 | 46.95 |

*Nitrogen of feces and vomitus, although not tabulated, included.

†Exclusive of amino acids.

‡Nitrogen received from two transfusions not included.

In Periods 7 and 8, Mixture Vx was given, and the caloric intake was increased. More nitrogen was retained, and there was a gain of 2.3 kilograms in weight. During the succeeding 10 days (Periods 9 and 10), the intake of nitrogen was entirely from food. Both the positive nitrogen balance and the gain in weight were somewhat greater.

A follow-up report from the patient 3 weeks later indicated continued improvement in general health and a continued rapid gain in weight.

## Comment

When sufficient calories are provided, the nitrogen obtained from the amino acid mixtures is well utilized. It should not be concluded that the nitrogen obtained from natural foods is better utilized, for the following reasons. First, the amino acid mixtures used may not be the optimal ones. Second, more than 20 per cent of the nitrogen contained in them is present in those certain unnatural isomers that are said not to be utilizable by rats for purposes of growth.[1] Third, the patient was obviously in better condition at the end of Period 8 than at the end of Period 6, when the second course of amino acid solutions was begun, and it may be argued that his metabolic machinery was functioning more efficiently at the end of Period 8, thus giving a certain advantage to Periods 9 and 10, during which the natural food protein was tested.

There was no significant change in the concentration of plasma protein during the metabolic study. It averaged 5 gm. per 100 cc. during Periods 1 to 3 and rose to 5.6 gm. during Periods 6 to 8.

Of the urinary nitrogen, the amount not excreted as urea and ammonia was higher during the periods of amino acid injection than it was during the period of comparable nitrogen intake from food protein. This increase has been recorded in dogs receiving amino acids or protein digest parenterally.[2, 14, 15] Its nature will be the subject of further investigation. It is apparently a function of the route of administration and not of the type of the nitrogen being administered, for it is not present in dogs when the same protein digest or amino acid mixture is given by mouth.

The glycine was originally added with the hope that it might furnish amino nitrogen for the in vivo synthesis of other nonessential amino acids. There is evidence from experiments in dogs that this hope is largely unrealized, but that the presence of glycine somewhat improved tolerance to the parenteral administration of the amino acid solutions.[16]

This report demonstrates the value in medical treatment of a synthetic mixture of pure amino acids given parenterally, but does not prove that this mixture contains all the amino acids required by man. At all times, as indicated in Table 2, nitrogen of unknown amino acid composition was being consumed. It is equally true that the oral diets used by other workers testing the amino acid requirements of human beings contain 5 to 10 per cent nitrogen of unknown composition.[18, 19] In another patient, to be reported soon, amino acid solution similar to Mixture Vx provided a positive nitrogen balance for a five-day period when it was the only source of exogenous nitrogen.

## Summary

A case is reported in which solutions of the amino acids essential for the growth of rats were given intravenously and subcutaneously without any clinical disturbance, and with satisfaction of the requirements of nitrogen equilibrium and formation of body protein. This fact is physiologically interesting and possibly of some practical importance in the treatment of patients.

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# MEDICAL PROGRESS

## SYPHILIS

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### Public-Health Aspects

Some extremely encouraging developments regarding the public-health aspect of syphilis, and particularly the sociologic facet, have been reported in publications during the last year. The Massachusetts law governing premarital examinations has not been in operation for sufficient time to allow a statistical survey of its usefulness. Talbot[1] has recently reported on the Connecticut law, with highly satisfactory findings. During the first seven years of its operation, 750 men and 690 women were found to have positive serologic tests for syphilis; this is equivalent to 14.1 per 1000 marriages. About 50 per cent of the patients diagnosed as having syphilis were unaware of their infection. Since the Connecticut law went into effect in 1936, the incidence of congenital syphilis has progressively decreased. The marriage rate dropped the first year, but since then it has increased steadily; in 1942 it was more than twice the 1932 figure. It may be said that the Connecticut law has been effective as a case-finding procedure and a measure for reducing the incidence of congenital syphilis. Physicians should have a greater incentive for taking routine serologic tests for syphilis. The education of the general public in regard to this disease should also be well served.

A consultation program on a statewide basis has been operating satisfactorily in New York. Kroll[2] reports on the operation of the plan, and it sounds quite workable. The state was divided into districts with a full-time consultant in each area. Local physicians were approached in two ways. Letters were sent out to all those in active practice; one of every eight made a response and the consultant visited their offices. The second approach was a visit to all physicians who had reported cases of syphilis under treatment, whether or not advice had been requested; one of every three of this group accepted assistance. Consultation may be obtained by mail or through a visit to the local physician's office with discussion of the case. An examination of the patient was carried out wherever possible, and such diagnostic procedures as dark-field examination, lumbar puncture and so forth were performed when requested. The problems of the participating physicians concerned late latent syphilis, the choice of drugs or the management of neurosyphilis in 50 per cent of the cases. The next 40 per cent of questions concerned the following in the order given: early syphilis, congenital infections, serologic interpretations, infectiousness, syphilis in pregnancy and cardiovascular syphilis. This program has apparently stimulated greater interest among general practitioners and served to educate them in more capable practice. The result has been greater co-operation with the public-health authorities. In addition to the consultation program, diagnostic clinics are operated in large centers.

From the purely sociologic standpoint and aside from other laudable aspects, California has taken two worth-while steps. A venereal-psychiatric clinic has been opened in San Francisco.[3] The purpose of this service is to provide re-education and readjustment for girls and women who have histories of promiscuous sex relations and who may spread or who are spreading venereal disease among the civilian population and armed forces. The socioeconomic background of these patients is studied, and every attempt is made to remedy their maladjustment. Emphasis is placed on rehabilitation and relocation of the patients through the co-operation of local agencies. A special court, the Separate Women's Court, has also been opened in San Francisco to meet the problem of sexually promiscuous women who are arrested.[4] Every effort is made to provide means for adequate referral for first offenders who present a potentiality for re-education and readjustment. The medical co-ordinator of the Separate Women's Court is the chief of the Division of Venereal Diseases. These measures seem most rational.

A new approach to the source-finding and suppression of venereal disease has been suggested by Williams.[5] His so-called "facilitation process" has been pursued in Vancouver, British Columbia, with considerable success. This approach to the control of venereal disease lies in the premise that the acquisition of a venereal disease is dependent on two factors: namely, the source of the infected person and the circumstances whereby the source is made accessible to the healthy person. Action dealing with the source has been a common procedure in all control campaigns. Action directed toward the "facilitators" to remove conditions rendering the source accessible is the key to Williams's plan. The facilitation process comprises those community conditions associated with the direct or indirect, witting or unwitting participants, usually for monetary gain of the third person, whereby persons suffering from common venereal disease are made accessible for intimate exposure to healthy persons. The facilitators or third-person participants, are madams, pimps and procurers with whom may be associated unethical

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physicians, lawyers, finance companies and real-estate agencies. Managers and owners of premises may also be in the ranks of the facilitators. The attitude of certain civic administrators, health departments and law-enforcement agencies may place the officials of these administrations, and also the public, in the position of being facilitators. Those engaged in the commerce of liquor are last, but by no means least. Dance halls, taverns, rooming houses and employees of these establishments, as well as taxicab-drivers, hotel clerks, bellhops and so forth, may be of great importance. Serious attention to such components of the facilitation process, as well as closing disorderly houses, has led to remarkable results in British Columbia. The Canadian Navy's monthly incidence of venereal disease on the West Coast has been only about half that on the East Coast. Canadian Army and Air Force statistics show a better record in the British Columbia district than in any other military area. These satisfactory figures substantiate Williams's claim for success in his campaign. He believes that "energy expended in the suppression of facilitation in a community is far more profitable from the public-health standpoint than the usual misdirected efforts at 'suppression of prostitution' which harassed the exploited, sick prostitute and left untouched the wealthy, healthy facilitator." This seems to be one of the most worthwhile campaigns for the control of venereal disease on record.

The widespread effect of the campaign of the United States Public Health Service to control venereal disease is reflected in innumerable articles. Practically every medical journal carries one or more publications in this vein from time to time, and there is considerable overlapping in their content. Attention can profitably be called, however, to police activities as outlined by Ness.[6] A National Advisory Police Committee appointed by Federal Security Administrator Paul V. McNutt unanimously endorsed an eight-point agreement as a national standard for law-enforcement officers throughout the United States. This agreement was drawn up jointly by the War Department, the Navy Department and the Federal Security Agency as the official federal policy for the control of venereal disease. Point 6 of the agreement recognizes prostitution as the chief source of venereal disease. In those communities that have clamped down on prostitution, there has been no crime wave or increase in rape cases. On the contrary, this action has frequently resulted in corresponding improvements in the criminal situation. The National Advisory Police Committee has recognized that the repression of prostitution is not the only method of control to protect the health and welfare of the armed forces, war workers and girls engaged in prostitution. An intelligent over-all war-protection program is necessary. Such a program must provide measures for the social and economic rehabilitation of the girls arrested, as well as the fundamental measures for attacking conditions which breed prostitution.

## Syphilis in the Armed Forces

Encouraging figures on the incidence of venereal disease have been published by Weber.[7] During World War I the rate was 86.7 per 1000. During 1941 the rate for the Army was 42 per 1000, and in the first six months of 1942 it had dropped to 38 per 1000. This is most heartening in view of the expected increase that has always accompanied the forays of Mars. Vonderlehr and Usilton[8] have published an analysis of serologic reports of nearly 2,000,000 men of draft age up to the end of August, 1941. This is the young adult male group, in whom the incidence of syphilis would be expected to be higher than that in any other. The rate of prevalence of syphilis, based on positive and doubtful blood tests among the selectees examined, was found to be 45.3 per 1000. The figures for white selectees in this group was only 17.4 per 1000. Most encouraging is the reduction in the incidence of venereal disease in the Navy.[9] The rate for all venereal disease was 80 per 1000 in 1940, 51 per 1000 in 1941 and about 36 per 1000 in 1942. The trend is thus downward by 50 per cent over the three-year period, and the Navy venereal-control officers can be justly proud of this result.

The British have apparently been having more trouble than have we, according to published figures. The increase in venereal disease since the beginning of the present war has been serious enough to demand special attention. The British public has been more reticent about publicity in regard to venereal disease than has the American public, and only recently have newspaper and magazine articles on the subject been printed. The Ministry of Health has issued a new defense regulation (No. 33B), under which it will be possible in certain cases to compel persons infected with venereal disease to undergo medical treatment.[10] Taking the number of civilian infections in syphilis alone, the most trustworthy test of the wartime increase, there were 5000 in 1939, 5600 in 1940 and 7300 in 1941. If to this are added the infections among British military services, the total increase in syphilitic infections amounts to 70 per cent. Venereal disease in Scotland showed an even greater increase, the incidence there having more than doubled since the outbreak of the war.[11] In Australia there had likewise been an increase in the incidence of early syphilis[12]; until fairly recently all soldiers in the Home forces having syphilis were discharged from the army as medically unfit and instructed to report to their own physicians or local boards of health for treatment. Re-enlistment was possible after a satisfactory course of treatment. Australian Army personnel having syphilis are not now discharged.[13] By a recent arrangement, infected soldiers are treated at special hospitals until non-infectious, and are then transferred to a company

for duty while their weekly injections are continued. In addition, an educational campaign is under way in the Australian Army.

### Syphilis in Industry

The man hours lost by workers in war industry as a result of venereal infections have reached serious enough proportions to warrant more active attempts to control syphilis in their field. Schwartz and Markel[14] have approached the problem from the standpoint of protecting the employee as well as the employer. The syphilitic worker, even in the primary or secondary stage of the disease, is a negligible source of infection to employees of the same sex. Neurosyphilitic patients should not be employed where lapses of consciousness, such as the dropping of explosives, may result in accidents. Workers having syphilis in the tertiary stage should not be employed where they are exposed to the action of nitrates and other nitrogenous compounds that have a marked effect on the vascular system or to lead and carbon disulfide, which affect the central nervous system. Even workers who have had adequate treatment for tertiary syphilis should not be exposed to the action of such compounds. Many occupational diseases can simulate syphilis in its various stages, and these are well portrayed in Schwartz and Markel's paper. This is a profitable publication for thorough study by all physicians engaging in industrial practice.

The Surgeon General of the United States Public Health Service has appointed an advisory committee to assemble current authoritative information and to formulate basic principles applicable to a program of venereal-disease control in industry. This committee has outlined the objective of such a program in regard to medical and public-health aspects and employees' problems, as well as those of the employer. Anderson et al.[15] elaborate on these objectives and outline the manner in which the plan can be operated. It is emphasized as of the utmost importance that the results of medical examination be considered confidential as between the worker and the medical staff. Venereal-disease forms should be filed in the medical department for the use of the medical staff only, and not in an open file. Employees found to have syphilis should be referred to a reputable source for medical attention and not discharged so long as the industrial physician is notified at regular intervals regarding continuation of treatment. The plant physician making a tentative diagnosis of syphilis or gonorrhea should without delay acquaint the appropriate health authority with the facts of the case. It is properly emphasized that there is no reason for denying employment to an applicant or for discharging an employee because a medical report has given evidence of syphilis or gonorrhea, provided the worker co-operates satisfactorily in the treatment program. Nelson[16] has written on the same problem in cogent fashion. One point well emphasized is that there is no relation whatever between the blood test and the infectiousness of syphilis. Nelson further states that it is to the best interests of both industry and society to put the infected person to work or to keep him at his job contingent on such treatment as may be necessary. This is safer than to dismiss him with completely unsupervised treatment or none at all. Nelson states that the use of the blood test as a key to employment in general, for the purpose of excluding those who may be dangerous in certain occupations, is as ridiculous from the point of view of public safety, and as unsound medically, as it is unjust. In many industries the problem is already being intelligently handled. How soon it is to be solved in others will largely depend on whether the well-informed physician or the uninformed layman is to determine the medical policy.

An example of a well-operated plan was published by Yeager.[17] Since 1934 the Remington Arms Company has been giving complete physical examinations to all employees, including a blood serologic test for syphilis. Applicants in a communicable or a contagious stage of syphilis cannot be employed, in conformance with the Connecticut state law. New employees in the noninfectious stage can be hired provided they take adequate treatment, a plant physician keeping check on this. Provision can be made for treatment at clinics for applicants who are unable to pay, and the employee's disease is kept strictly confidential. Applicants or employees in a communicable stage are considered for employment after they have been rendered noninfectious by treatment. Although the Selective Service statistics show that Connecticut has the lowest percentage of syphilis in any state, the incidence among the employees of the Remington Company's Bridgeport works is even lower. The employees are most grateful to the company for making it possible to diagnose the condition, particularly those who had no previous knowledge of their infection or thought they were cured.

The control of venereal disease in industry will save time and money for all concerned, as pointed out by Anderson.[18] It will also achieve a higher standard of efficiency and increase the industrial worker's earning capacity and life expectancy. The syphilitic blind cost society about $10,000,000 a year, and paretic patients in state institutions cost another $6,500,000. Congress appropriated $12,500,000 for the control of venereal disease in 1943, and the states will raise some $7,000,000. To each of these sums industry will contribute liberally through taxes. From the cost angle alone, therefore, industry has a considerable stake in venereal-disease control. The state health departments may have to provide mobile facilities for the employees in the smaller plants that have no regular medical service. One such department has a blood-test trailer operating among small plants and communities.

It should be pointed out that the safest worker regarding the spread of syphilis is one with a positive serologic test for syphilis who is under treatment, after passing the infectious stage; he or she is also immune to reinfection. If venereal-disease control can be furthered by education of industrial workers, and industry itself can be shown the fallacy of discharging workers on the basis of a positive serologic test alone, a great step will have been taken. Strikes in war plants arouse the indignation of the public because of wasted time and money and loss of production. Venereal disease can be responsible for these same losses.

## Experimental Research

The vast amount of plasma in use by the armed forces and the rapid rise in the popularity of blood banks increase the importance of a study concerning the survival of *Treponema pallidum* in the various preparations. Ravitch and Chambers[19] investigated this problem in regard to frozen plasma, with experiments on animals. They were able to show that human and rabbit plasma heavily inoculated with *Tr. pallidum* and frozen at –20°C. for forty-eight hours or longer is not infectious for normal rabbits.

A study of the similarities of several representative types of bismuth preparations used in the therapy of experimental syphilis has been reported by Clausen, Longley, Green and Tatum.[20] Five bismuth compounds in common use were employed, with both intramuscular and intravenous administration to animals. Their toxicity was studied and the therapeutic efficiency of each was computed. The similarity of the minimal curative dose, regardless of the route of administration, and the similarity in the toxicity of the various preparations when given intravenously suggested that basically all bismuth preparations ultimately act in a common form rather than in the form in which they are injected. The effect of ammonium chloride on the mobilization and excretion of bismuth in normal and syphilitic rabbits was studied by Brown, Kolmer and Rule.[21] In the presence of massive doses of bismuth subsalicylate this effect of ammonium chloride may increase the toxic effects of the bismuth. In the treatment of acute testicular syphilis of rabbits, the increased mobilization of bismuth was without therapeutic value. In human beings, however, the opinion was expressed that this increased mobilization of bismuth may lead to an enhanced therapeutic effectiveness. It was pointed out that since acidosis increased the toxic effects of bismuth, it is not advisable to administer ammonium chloride to syphilitic persons predisposed to the acidotic state.

It would be ideal to have an arsenical preparation that could be used effectively by oral administration in the treatment of syphilis. Rosenthal[22] has studied Mapharsen in this respect. Mice infected with a trypanosome were cured by oral doses. Rabbit syphilis was then attacked in the same fashion, with satisfactory results. Glutathione and cysteine were found to decrease the toxicity of Mapharsen without effecting its therapeutic activity, and the drug was better tolerated when one of these was given. Similar work was carried out by Brown, Kolmer and Rule.[23] Working with rats, these investigators found that the trivalent arsenical drugs were far less toxic when given by oral administration than when injected intravenously. Mapharsen was least toxic by a large margin. Rabbits with acute testicular syphilis were then treated by the oral administration of trivalent arsenicals. In terms of arsenic administered, it was found that the therapeutic effectiveness of Mapharsen by oral administration is higher than in the case of arsphenamine and neoarsphenamine. The same group[24] then studied the toxicity and therapeutic effectiveness of arsenical preparations by intramuscular administration. Here again, Mapharsen was found to be of lower toxicity than the other drugs and of high therapeutic effectiveness. These results suggested that the intramuscular injection of Mapharsen in sterile peanut oil may prove to be of value in the treatment of human syphilis. A schedule of five daily intramuscular injections was projected for a massive arsenotherapy schedule for early syphilis. If clinical experiment should bear out this possibility, many of the dangers of massive therapy might be reduced.

There has been considerable disagreement regarding primary optic atrophy in neurosyphilis. It seems possible that visual damage in treated cases may be due to the syphilis itself, to the therapeutic agent or to a combination of factors. Longley, Clausen and Tatum[25] studied the experimental production of primary optic atrophy in monkeys, which were chosen since their eyes have been found to resemble those of human beings more closely than do the rabbit's. Five arsenical compounds were administered intravenously to different groups of animals in gradually increasing doses at weekly intervals. In these experiments, blindness was produced in monkeys in varying degrees by each of the drugs. The authors believe that this work provides an experimental basis for detecting the blinding potentialities of arsenical compounds for man. It also provides the means for a study of prophylactic procedures designed to reduce or eliminate optic atrophy as a sequence of chemotherapy for neurosyphilis. Tryparsamide amblyopia was studied by McDermott, Webster, Baker, Lockhart and Tompsett[26] from the standpoint of nutritional degeneration of the optic nerve in rats. Deficiencies of various vitamins were produced in certain groups of animals, and these, with normal rats, were treated with tryparsamide. Only in the presence of adequate amounts of vitamin B complex (yeast) and vitamin A (cod-liver oil) did rats fail to develop degeneration of the optic nerve. This was found to be true whether or not they were treated with tryparsamide, although the latter in-

tensified the degeneration. The implications of this work seem obvious.

### Pathology

Autopsy material of the last twenty-five years at Yale University School of Medicine has been analyzed for syphilis by Rosahn and Black-Schaffer.[27] Five thousand three hundred autopsies were performed during this time. Those done on persons twenty years of age or over numbered 3907, and of these 380 (9.7 per cent) had clinical, laboratory or post-mortem evidence of syphilis. In this group of 380 syphilitic patients there were 156 (41 per cent) with morphologic lesions of syphilis. Ninety (58 per cent) of these patients with anatomic lesions died primarily as a result of their syphilis. When the material was analyzed from the standpoint of sex incidence, it was found that women appeared to have a significant resistance to the tissue changes of late syphilis, and that this was independent of race. When the syphilitic and nonsyphilitic portions of this autopsy material were compared, it was found that the mere presence of syphilis significantly reduces longevity, regardless of whether or not tissue lesions result. Twenty per cent of nonsyphilitic patients survived after the age of seventy, as against only 10 per cent of those with syphilis. Life-insurance actuaries would do well to review these findings.

### Syphilis and Cancer

The prevalence of syphilis among a sample series of 7761 cancer cases was studied by Levin, Kress and Goldstein.[28] Of the 3151 male patients, 3.2 per cent were found to have been reported as syphilitic, and among 4610 female patients, 1.7 per cent had syphilis. Males with cancer of the tongue showed a greater prevalence of syphilis than did those with cancer of other sites, in the ratio of 5:1. Among females with cancer of the uterine cervix, the corresponding ratio was 3.5:1. This higher prevalence of syphilis is similar in both instances to that reported in other studies and has long been recognized.

### Morphologic Diagnosis

An interesting variation in dark-field microscopy technic is suggested by Witlin.[29] This author recommends examining the slide under the low and high-dry objectives before applying oil to the coverslip. Time is thereby saved in locating the organism, and it can then be properly identified by observation under the oil-immersion lens. The importance of dark-field examination of lesions of the cervix is emphasized by Sharp, Alexander and Schoch.[30] It is stressed that although a cervical lesion may appear to be traumatic or merely an exacerbation of chronic cervicitis, a dark-field examination may reveal spirochetes. This applies particularly to the examination of contacts of known syphilitic patients and of patients with seronegative primary syphilis. The use of the dark-field in the diagnosis of secondary syphilis has been portrayed by Agee.[31] The employment of this technic in primary lesions of syphilis, genital or otherwise, and in moist papules is generally recognized as an essential diagnostic procedure. It is the advisability of searching for spirochetes in other types of skin lesions that Agee emphasizes. This is obviously intelligent when one considers that the presence of positive serologic tests with skin lesions suspected of being those of syphilis does not necessarily prove the case as secondary. Also, the beginning of treatment can be expedited by obtaining a positive dark-field reaction without waiting for a positive serologic report. Dry or closed secondary lesions can be abraded vigorously by means of a scalpel or dry gauze. If serum does not exude freely, it may be necessary to squeeze the area to express such material.

From time to time various stains for *T. pallidum* have been described. These procedures are useful under some circumstances where a dark-field condenser is not readily available or where the patient cannot be transported. Smears can be obtained in outlying communities and properly examined elsewhere within a comparatively short time. Perrin[32] describes such a method, which in his hands has proved simple, rapid and reliable.

### Reinfection

The problem of reinfection versus superinfection versus recurrence of the infectious phase has always been a source of considerable discussion. There has been an apparent increase in reinfections since the advent of so-called "massive therapy," as will be shown below. This has brought up the advisability of reviewing the criteria of reinfection, and several papers on this subject have appeared. Schoch and Alexander[33] have expressed a somewhat altered concept of reinfection in view of their experiences, and record 10 cases. Four patients sustained reinfection following orthodox antisyphilitic therapy. Six of 103 patients were reinfected following a ten-day course of intensive arsenotherapy (1200 mg. of Mapharsen) for early syphilis. The details of these cases are reviewed, and for the most part they fit well into the category of reinfections. The authors state that whether or not the six cases of reinfection following intensive therapy are acceptable as such, they serve to emphasize the importance of developing new and more rapid epidemiologic approaches to syphilis when short-term intensive schedules of treatment are used. Schoch and Alexander offer a hypothesis to explain the fact that more reinfections seem to be occurring. This explanation intimates that patients with early syphilis treated by intensive methods are prevented by treatment from developing any immunity against reinfection, that the chemotherapeutic prophylactic effect of intravenous arsenotherapy disappears within a brief time after treatment ceases, and that such patients are prone to expose themselves so soon to the infectious

sex partner from whom the original infection was acquired that this contact still remains infectious. One may, of course, wonder whether syphilitic patients are so constant in their sexual behavior. The above theory also indicates a marked inadequacy of contact tracing. Moore[34] has commented editorially on the same problem. He quotes Stokes's seventeen requirements for so-called "indisputable" reinfections. Moore reduces the criteria to three points, summarized as follows: adequate proof that the patient had syphilis prior to the recurrence of the supposed second infection; development of a primary lesion after a suitable interval following treatment for the previous infection and at a different site from the preceding primary lesion (spirochetes must be demonstrated); and the serologic test for syphilis, which must be negative at the time of the supposed reinfection and must, while the patient is under observation with treatment purposely withheld, become positive, or the patient must develop proved secondary syphilis. Although reinfection is relatively rare in patients treated by standard methods, Moore states that the introduction of intensive arsenotherapy has apparently, "perhaps as much as twelvefold," increased their incidence. He further states that existing knowledge does not permit a definite decision in all cases regarding the question of reinfection, superinfection or relapse. Moore is somewhat critical of the hypothesis used by Schoch and Alexander[33] to explain the increase of reinfection. He suggests other possibilities. First, standard prolonged treatment is less likely to be curative in the biologic sense (in the elimination of the last remaining organism). Second, the standard prolonged method permits the simultaneous development of immunity, which persists after biologic cure is achieved, whereas intensive arsenotherapy prevents or abolishes such immunity. Third, there may be a slow absorption over months or even years from depots of bismuth deposited under the conditions of standard treatment. This may act as a chemotherapeutic prophylaxis against subsequent reinfection, since the protective effect of bismuth has been demonstrated both in animals and in human beings. Patients treated with massive therapy have usually received only arsenic. Whether one of these explanations or some other is the correct one, the apparently increased incidence of reinfections after intensive arsenotherapy is an added incentive to the search for a safer method of intensive treatment.

For those who would review the criteria of reinfection in syphilis, an article by Shaffer[35] seems clear, and detailed enough to be extremely instructive. An excellent tabulation of the criteria is presented. The author also suggests somewhat altered requirements for the establishment of reinfection in cases receiving intensive treatment. He believes that supposed reinfection occurring within six months after intensive treatment is completed cannot be differentiated from potential superinfection.

*(To be concluded)*

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# CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

## Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

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## CASE 30041

### PRESENTATION OF CASE

A forty-nine-year-old housewife entered the hospital because of jaundice of four days' duration.

The patient was in fair health until about five weeks before admission, when she began to feel tired and run down. She developed a gnawing pain in the right upper quadrant. There was some numbness of the fingertips, and stiffness of fingers in the mornings. About two weeks before admission she had a shaking chill, with fever of 102°F. associated with sore throat, headache, running nose and generalized aches and pains. Ten days prior to entry, she had a crampy pain in the right upper quadrant lasting for a few minutes. The malaise, anorexia and coryza persisted. She had a cough productive of yellowish-brown mucoid sputum. The temperature was about 101°F. Four days before admission she noted jaundice of the skin and scleras. At the same time the urine became dark yellow, and the stools a light tan. She developed a severe headache and had waves of nausea but no vomiting.

Twelve years before her present admission the patient was admitted to another hospital for functional bleeding. She received 1400 milligram-hours of radium. Ten years later she was readmitted to the same hospital for essentially the same complaint. A dilatation and curettage was of no value, and about six months later she was given 2000 milligram-hours of radium. This was followed some months later by radiation proctitis. She was then transferred to this hospital, where a hysterectomy was performed ten months before her present entry, the diagnosis being pyometrium. At that time she also had a bilateral femoral-vein ligation following thrombophlebitis of the right calf. The proctitis improved with the removal of fecal impactions, and she was discharged well, seven months before the present admission.

Physical examination showed an obese woman in no distress. There was moderate icterus of the skin and scleras. Small petechiae were peppered over the lower abdomen, left arm and lower back. The axillary and inguinal lymph nodes were small and nontender. The heart was percussed 1 cm. to the left of the midclavicular line. The sounds were regular and of good quality. There was a soft systolic murmur, heard loudest at the apex. The lungs were clear. The abdominal wall was pendulous. The liver edge was palpable three or four fingerbreadths below the costal margin. It was firm, smooth and slightly tender. The spleen was palpable three fingerbreadths below the costal margin; it was not tender. Pelvic examination showed a bilaterally lacerated cervix covered with an atrophic mucosa. There was slight tenderness in the right vault, but no masses could be palpated.

The blood pressure was 140 systolic, 75 diastolic. The temperature was 98.6°F., the pulse 72, and the respirations 24.

Examination of the blood showed a red-cell count of 4,300,000, with 12.5 gm. of hemoglobin. The white-cell count was 4000, with 72 per cent neutrophils, 22 per cent lymphocytes and 6 per cent monocytes. The platelets were slightly diminished, the red cells showed slight variation in size and shape, with many target cells, and the neutrophils showed a shift to the left. A blood Hinton test was negative. The urine was dark amber and acid, with a specific gravity of 1.020; there was no albumin, but a ++ bile test. It was positive for urobilinogen in 1:20 dilution (normal, 1:10). The stools were light tan and guaiac negative. The bleeding time was 6 minutes, and the clotting time 15 minutes. A fragility test showed beginning hemolysis in 0.40 per cent and complete hemolysis in 0.28 per cent sodium chloride solution. A tourniquet test gave 25 petechiae per square centimeter after fifteen minutes with a pressure of 100 mm. of mercury (normal, 6 to 20). The blood sugar was 104 mg. per 100 cc. The direct van den Bergh was 6.6 mg., the indirect 9.6 mg. The total protein was 5.2 gm. per 100 cc., with 3.2 gm. of albumin and 2.0 gm. of globulin. The nonprotein nitrogen was 31 mg. per 100 cc. The prothrombin time was 27 seconds (normal, 18 seconds). The hematocrit was 46.5. A cephalin flocculation test was ++++ in twenty-four hours and ++++ in forty-eight hours. There was 100 per cent retention of bromsulfalein.

Plain films of the abdomen showed several ring shadows in the right upper quadrant that had the appearance of gallstones. A gastrointestinal series and films of the chest were negative.

The patient was given a high-carbohydrate, high-vitamin B, low-calorie and low-fat diet, supplemented daily by 500 cc. of intravenous dextrose. In the next few days the jaundice definitely increased. She had several, occasionally severe but usually moderate colicky attacks of right-sided abdominal pain. The pain was mostly in the upper quadrant and on one or two occasions radiated to the shoulder.

On the tenth hospital day she became orthopneic, with a feeling of substernal oppression, and was

*On leave of absence.

forced to sit up. There was profuse sweating. This episode presumably lasted for a few minutes. The temperature was 100°F., the pulse 96, and the respirations 24. The white-cell count was 5200, with 82 per cent neutrophils. The urine had a + test for albumin and a ++ test for bile. The stools became brown and remained so. The direct van den Bergh was 12.7 mg., the indirect 17 mg. The prothrombin time was 49 seconds (normal, 20 seconds). The hematocrit was 40.0, and the nonprotein nitrogen 17 mg. per 100 cc.

The patient's condition became progressively worse. She was nauseated, retched considerably and vomited occasionally. She was given daily intravenous dextrose and repeated transfusions. On the sixteenth hospital day the van den Bergh was 8.2 mg. direct, and 13.8 mg. indirect. The stools became guaiac positive. The urine gave a +++ test for albumin and a ++ test for bile, and was positive for tyrosine crystals (Morner's test).

She died on the eighteenth hospital day.

### Differential Diagnosis

Dr. Marian Ropes: May we see the x-ray films?

Dr. George W. Holmes: The gallstones are obvious. The position of the gallstones gives some idea concerning the position of the lower border of the liver. You can vaguely make out the liver shadow. It is not enlarged so far as I can see, nor abnormal in shape. In this film the diaphragm seems to be quite high on the right side so that even though the lower border is not unusually low, the liver might still be somewhat enlarged. It is also possible that the film was taken at the end of expiration rather than of inspiration. I see nothing abnormal in the lung fields. The heart shadow is well within normal limits, both in size and shape.

As I understand the story the patient received radium treatment and was said to have had proctitis following it. Apparently an effort was made to study the rectum and lower sigmoid by means of a barium enema, a rather careful search having been made for any abnormality in that region, but I should say that this is a rather normal looking colon throughout. We have some films of the stomach, including the duodenal loop, that appear to be normal. In the cases with serious complication following heavy radiation to the pelvis, the organ most likely to be injured is the small bowel. Patients will stand a good deal of injury to the large bowel and recover, but the same amount of injury to the small bowel often causes considerable difficulty. There is no indication here of such injury — no collection of gas and no dilated loops of small bowel suggesting obstruction, such as might occur after heavy radiation.

Dr. Ropes: This case presents a picture with various confusing features. It is apparent that the patient had severe liver-cell damage, and it is also probable that she had some obstruction to the biliary flow. I judge that her death was due fundamentally to the liver damage. The underlying etiology and sequence of events leading to this final picture, however, are not equally clear. Various etiologic possibilities should be considered. A malignant neoplasm, either primary or secondary in the liver, or primary in any part of the biliary system, seems unlikely in view of the rapid course of the disease, the variation in jaundice, and the marked evidence of liver-cell damage. Pylephlebitis, idiopathic hepatitis, cholangitis, cholelithiasis and cholecystitis should be considered. Before discussing these possibilities however, it might be well to summarize the evidence indicative of the extent to which the jaundice was due to liver-cell damage and the extent to which obstruction may have played a role.

The clinical evidence gave little information in this respect except the fact that bile in some quantity reached the gastrointestinal tract at all times during the disease,with resulting tan or brown stools and with normal bilirubin in the urine. In the laboratory evidence one finds definite indication of liver damage as indicated by the tyrosine crystals in the urine; the high cephalin flocculation test is presumably further indication of severe liver-cell damage, as is perhaps the leukopenia. The low globulin is a surprising finding and helps me not at all in differentiation in this respect. The exceptionally high bromsulfalein retention would not have been found unless there had been severe liver-cell damage, even if obstruction were present. The van den Bergh gives a suggestion of obstruction to biliary flow. A high direct van den Bergh, particularly as high as it was in this case, is unlikely in pure parenchymatous liver disease. I am told that a direct-indirect ratio of 60 to 80 — this patient had 70 — is suggestive of obstruction, whereas in pure parenchymatous liver disease the ratio rarely goes over 50. How well corroborated that is, I do not know.

With this evidence I should like to return to the etiologic possibilities. Pylephlebitis must be considered. It is intriguing to consider whether one could thereby relate the pelvic inflammation — the pyometrium — to the present illness. It would be unusual to have an asymptomatic period of six months, and an absence of fever and leukocytosis. The marked evidence of liver damage is difficult to explain on the basis of pylephlebitis. Idiopathic hepatitis and cholangitis would explain most of the picture. The early onset of pain in the right upper quadrant and the recurrent attacks of moderately severe colicky pain are unusual in this condition but not entirely inconsistent with it. The gallstones cannot be overlooked. So far as we know, they were rather large and presumably in the gall bladder. Gallstones, particularly if in the common duct, with some obstruction and with some cholangitis, could form the basis for this terminal picture. The presence of the splenomegaly raises the question of an

underlying cirrhosis. I believe, however, that the enlargement of the spleen could be ascribed to the severe liver damage. The tender large liver — at least clinically large — and the large spleen are consistent with pylephlebitis, with idiopathic hepatitis or with hepatitis associated with cholelithiasis.

In conclusion I think that this patient had severe parenchymatous liver disease and that she also had cholelithiasis. Whether the former could in any way be related to the latter etiologically, I do not know. It seems somewhat improbable. I also doubt that she had pylephlebitis as an underlying cause of the severe liver disease.

Dr. J. H. Means: I saw this patient every day while she was in the hospital and followed her carefully. Our line of reasoning followed Dr. Ropes almost exactly and led to the same diagnosis. We believed that she died of severe parenchymatous liver disease, a hepatitis of some sort. We did not know of what variety. We also tried to connect it with the pelvic sepsis and wondered if she had pylephlebitis, but in my note I stated that I thought that that was unlikely because she had had a considerable interval of good health in between. The question of cirrhosis was considered. The size of the spleen was interesting. I thought the liver was enlarged when she first came in, and I am interested to know what the pathologist has to say about that. The clinician and radiologist often have different views about the size of the liver, but the pathologist is able to settle the matter because he can weigh it. I thought that the liver was firm and smooth but could not feel a definite edge.

The impressive thing on the ward was the steady downhill course, the patient becoming sicker and sicker every day in spite of all we could do. Dr. Chester M. Jones saw her several times, and Dr. Arthur W. Allen was asked to see her because the question arose whether she should be explored, but that was decided against. Dr. Jones laid a great deal of weight on the color of the stools. Indeed, he said to me one day, "If the stools remain brown, do not let the surgeons do a laparotomy." They remained brown, and the surgeons did not want to do a laparotomy. We thought that the gallstones had little or nothing to do with the picture in all probability. She had not taken any medicine that we could recognize as a liver toxin, so we called it hepatitis of unknown origin. We did think at the end that she might have had acute yellow atrophy, although we could not prove it. We also thought of the possibility of an acute yellow atrophy that supervened on a cirrhotic liver but could not establish that diagnosis.

Dr. Jacob Lerman: Did the liver change in size?

Dr. Means: I cannot answer that. I do not know that we proved that it did.

Dr. Paul Zamecnik: Was catarrhal jaundice considered?

Dr. Means: Yes, at entry. She did not appear to be particularly sick and we thought that that was a reasonable diagnosis to consider. The blood picture was consistent with it. In fact she was almost too well to have catarrhal jaundice. She rapidly became sicker and sicker and we abandoned that diagnosis as inadequate.

Dr. Zamecnik: It is occasionally followed by hepatitis.

Dr. Means: That is true. Catarrhal jaundice is hepatitis, is it not? It is really just a matter of degree. We wondered when she died if we had treated her adequately. We had given her a diet low in fat and high in everything else, pushed with vigor. Dr. Jones thought that we had done everything possible.

### Clinical Diagnoses

Intrahepatic disease.
Acute yellow atrophy?
Cholelithiasis.

### Dr. Ropes's Diagnoses

Parenchymatous liver disease.
Cholelithiasis.

### Anatomical Diagnoses

Subacute yellow atrophy of liver.
Splenomegaly.
Ascites.
Cholelithiasis.

### Pathological Discussion

Dr. Benjamin Castleman: The autopsy showed a liver of normal size, weighing 1400 gm. It was greenish brown and extremely friable; as one touched it, it broke. It had on the surface a few elevations, as if some attempt at regeneration had occurred. From the gross appearance we thought that it was an acute yellow atrophy of the liver.

Microscopic examination showed that practically all the liver cells had been destroyed. There were a few small islands of regeneration, so that this was perhaps a subacute yellow atrophy. The point that Dr. Means brought out — namely, that catarrhal jaundice is merely a mild form of acute yellow atrophy — is probably correct. We believe that it is exactly the same disease. Aspiration biopsies of the livers of patients ill with catarrhal jaundice have shown diffuse hepatitis, with inflammatory cells in the early stages, followed by areas of necrosis and finally by connective-tissue proliferation.[1] If the disease is not severe, the patient gets well; if severe, death is due to acute yellow atrophy or subacute yellow atrophy, depending on how long the course runs.

The spleen was enlarged, weighing 550 gm., the usual finding in atrophy of the liver. There were

about 400 cc. of bile-stained ascitic fluid. All the gallstones were within the gall bladder, which was thin walled and normal appearing. There was no evidence that a stone had ever passed down the bile duct.

DR. HOLMES: Was there anything in the bowel to indicate injury from radiation?

DR. CASTLEMAN: The only evidence we found was that the sigmoid was adherent to the anterior abdominal wall. There was no evidence of stenosis of the intestinal tract. There were many petechial hemorrhages throughout the body, apparently due to the severe jaundice.

DR. FULLER ALBRIGHT: Do you think that catarrhal jaundice can occur without hepatitis? We have had two cases recently that had no evidence of liver damage.

DR. CASTLEMAN: No; I believe one should find hepatitis with catarrhal jaundice. At least the work done in Copenhagen[1] has shown that.

DR. ALBRIGHT: These two patients were operated on, and biopsies of the liver showed nothing.

DR. CASTLEMAN: I am surprised at that.

DR. ALBRIGHT: At least that is what your department said.

DR. CASTLEMAN: I suppose in the early stage there could be marked edema and granularity. Perhaps we had better review those slides.

DR. ALBRIGHT: The original idea was that catarrhal jaundice was caused by a duodenitis in the region of the ampulla of Vater, with the production of a mucous plug in the bile duct.

DR. CASTLEMAN: That was disproved by Eppinger[2] years ago, who found liver-cell destruction in four soldiers dying of injuries while having catarrhal jaundice. I do not believe that it has anything to do with the bile duct.

DR. ALBRIGHT: It is a matter of definition. You are willing to grant that there is such a thing as infection of the bile ducts that clears up?

DR. CASTLEMAN: Yes, but that is cholangitis, which does not necessarily involve the liver.

DR. ALBRIGHT: Are not a lot of things that we call catarrhal jaundice due to that?

DR. CASTLEMAN: No. Usually one finds a stone as a basis for it. Is that not your experience, Dr. McKittrick?

DR. LELAND S. MCKITTRICK: Almost always. If a diagnosis of cholangitis is made I assume the presence of obstruction of some kind, usually a stone.

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## CASE 30042

### PRESENTATION OF CASE

A ten-year-old schoolboy entered the hospital because of persistent pain in the left arm.

Approximately three years prior to admission the patient had a series of diphtheria toxin-antitoxin inoculations. At about that time he began to complain of pain and soreness in the left upper arm at the shoulder, particularly associated with vigorous movement of the arm or pressure applied to the shoulder. Because of the recent injections no importance was attached to his complaints. One and a half years prior to admission, because the left arm had not developed so well as the right and since the shoulder pain persisted, he was taken to the family physician but no definite diagnosis was established. Eight months before entry the family physician found a swelling of the soft tissues about the left shoulder but no mass was felt. The swelling increased, and after a short stay in a community hospital the patient was sent to this hospital.

At the time of admission the patient complained of frequent episodes of a rather dull, aching type of pain along the left upper arm and over the left shoulder. This pain was aggravated by pressure or by sudden jarring but not by motion of the arm. There were also occasional sharp shooting pains along the outer aspect of the upper arm, especially following pressure over the shoulder. The patient was left handed and was able to carry out all movements with this arm except "throwing a ball." The patient had recently noted trembling of the left hand and fingers after muscular exertion of that arm.

The family and past histories were negative. The patient was born at full term and no injuries were noted.

Physical examination disclosed a well-developed but thin boy who seemed quite comfortable. The heart, lungs and abdomen were normal. The arms were equal in length. The right upper arm was 19 cm. in circumference; the left was 16.1 cm., and seemed somewhat less well developed. At rest the latter was carried with the elbow and wrist in partial flexion. The grip was weaker in the left hand than in the right, and there was less strength in the forearm. The left shoulder could not be rotated, but other motions of this extremity seemed normal. On the left, there was a tremor of the fingers and hand on an attempt to maintain extension; sensation in the arm was normal, and the reflexes physiologic.

An extremely firm, poorly defined mass about 6 cm. in diameter was felt under the midportion of the left clavicle that seemed attached to this bone. There was tenderness over this area and in the anterior portion of the left axilla, and tenderness to deep palpation over the upper arm. The mass did not involve the skin.

The blood pressure, temperature, pulse and respirations were normal.

Examination of the blood showed a hemoglobin of 95 per cent, a red-cell count of 4,400,000 and a white-cell count of 7900, with 60 per cent neutrophils. The urine was normal. A blood Hinton test was negative.

Stereoscopic x-ray films of the left shoulder showed the clavicle to be normal. There was a well-defined soft-tissue mass in the supraclavicular area on the left that extended downward behind the clavicle and apparently into the space between the scapula and the chest wall (Fig. 1). This mass showed several flecks of calcification. The lowermost areas of calcification lay close to the undersurface of the scapula. A questionable separate mass was seen in the axilla. The undersurface of the scapula seemed thinned by the mass. X-ray films of the chest, abdomen and long bones showed no evidence of pathology.

An operation was performed on the thirteenth hospital day.

## Differential Diagnosis

Dr. Carroll B. Larson: The initial complaint was pain in the left arm at the shoulder, especially on vigorous movement or by pressure on the shoulder. In the subsequent history I am not sure when they say "pain over the shoulder" whether they mean over the scapular joint. It might make a difference.

Dr. Robert R. Linton: I believe it was directly over the shoulder.

Dr. Larson: Do you recall whether it was worse at night than during the day, which is characteristic of deep bone pain?

Dr. Linton: I do not believe that it was.

Dr. Larson: Apparently there was no mechanical obstruction to the usual motions of the arm. The fact that he could not throw a ball, however, suggests that there was some difficulty.

This story does not suggest a lesion in the region of the epiphysis or a lesion disturbing the blood supply because of no inequality in arm lengths at the end of a three-year period. The difference in the circumferences of the two arms could have come from lack of use of the left arm rather than from the lack of development.

At rest the arm "was carried with the elbow and wrist in partial flexion." I am not sure what to make of that. It may be possible that, with a mechanical difficulty in the shoulder, such a position was a comfortable one for carrying the arm. The inability to rotate the left shoulder might have been because of pain or mechanical obstruction.

The tremor could be accounted for by lack of muscular development. Anyone with weak muscles cannot sustain a position for any length of time without tremor.

Perhaps we might see the x-ray films at this point. There is a fullness in the supraclavicular region that does look like a "holding forward" of the shoulder, which gives it a shortening in the anteroposterior view. The joint may or may not be deformed.

Dr. Milford Schulz: The chest is normal except for the deformity of the left shoulder girdle. Here we see the soft-tissue mass extending above the clavicle. These probably are the areas of calcification referred to. In addition one cannot see any bone structure in the body of the scapula. Of course the scapula is normally quite thin in this area, and that may be the reason. From the x-ray films there is no way of knowing whether the calcification is in the soft tissue or represents new-bone formation.

Dr. Larson: The child was perfectly well following the toxin-antitoxin injections. On that basis we

Figure 1. *Roentgenogram of Left Shoulder Showing Soft-Tissue Mass in Supraclavicular and Subscapular Regions.*

can exclude tuberculosis and chronic infection, which might have originated in bone and ended up in a soft-tissue mass giving this picture. The chest was negative and there was no cough or pain referable to the chest, so that we can probably exclude anything coming from the chest.

That leaves us with a tumor in this region but we are not sure whether it arose from bone or from the tissues around the bone. The fact that it was producing symptoms for three years is against a malignant tumor, but does not exclude it. Let us consider the bone tumors that occur in a child of this age.

With Ewing's tumor one would expect more new-bone formation. Lymphoblastoma occurs in this group of children and this is one of the locations in which it can occur; frequently the tumor exteriorizes

itself from the bone and produces a soft-tissue mass. In this boy there was little bone destruction compared to the size of the mass. With malignant lymphoma there is usually some clinical evidence of malignant disease, such as cachexia and marked anemia. I cannot, however, exclude lymphoblastoma as a possibility. Giant-cell tumor can be excluded almost immediately. There was not enough bone destruction, and the patient was in the wrong age group. A chondrosarcoma can occur in this area, and there may be areas of calcification within it. The mass may have developed from malignant degeneration in a chondroma. I cannot exclude that. Fibrosarcoma must also be considered. This mass overlay an area where the subscapularis muscle originates, and a soft-tissue tumor like a fibrosarcoma can develop in the subscapularis itself. In a primary nerve tumor one would expect more persistent pain and a greater number of neurologic findings.

Cartilaginous exostoses might fit in with a bone condition of this sort. It is most unusual for exostoses to reach this point of growth without producing more pronounced mechanical symptoms than this boy had, and there should be more evidence of new-bone formation. Hence, I exclude this diagnosis.

That leaves us with malignant tumor, even though the patient did not show constitutional signs of malignancy after three years. I believe that it was of the chondroblastic type, but it might have been fibroblastic or lymphoblastic.

DR. WILLIAM B. BREED: I do not understand whether you believe that the tumor originated in the bone.

DR. LARSON: As I stated before, the decision is difficult. The tumor could have originated in the bone and could have exteriorized itself, or it could have produced the entire x-ray picture by external pressure. I favor the former.

DR. LINTON: We were indefinite in our minds preoperatively concerning where the lesion originated. I rather thought that it was a malignant lesion, which would necessitate a shoulder-girdle amputation. Dr. J. C. White saw the boy because the question of nerve tumor was raised. It was decided that, if the tumor was not malignant, he would try to remove it by lifting the brachial plexus and the supraclavicular vessels. He started the operation by dividing the clavicle and exposing the tumor. It was obvious that the tumor was malignant and I completed the operation by doing a shoulder-girdle amputation and removing the entire clavicle. I did a block dissection and did not try to determine where the tumor had arisen. It was our feeling that it probably arose from the brachial plexus. Extensive dissection of the cervical lymph nodes was also performed since some of the nodes in the posterior triangle were enlarged and appeared to be involved. The roots of the brachial plexus were divided close to the intervertebral foramens.

### CLINICAL DIAGNOSIS

Tumor of clavicle (neurofibroma?).

### DR. LARSON'S DIAGNOSIS

Chondrosarcoma of scapula, low grade (possibly fibrosarcoma of subscapular region or lymphoblastoma of scapula).

### ANATOMICAL DIAGNOSIS

Neurogenic fibrosarcoma of subscapular region.

### PATHOLOGICAL DISCUSSION

DR. BENJAMIN CASTLEMAN: The tumor was large and fibrous and measured 14 by 9 by 6 cm. There was erosion of the scapula and of the clavicle, but it seemed to us to be the type of erosion that results from long-standing pressure against bone. There was no direct invasion of bone. The mass did, however, invade some of the surrounding muscles.

Microscopically it was a low-grade neurogenic fibrosarcoma, that probably arose from one of the branches of the brachial plexus. The regional lymph nodes were negative.

DR. LINTON: From the surgical point of view, if it was a low-grade malignant process, such as a fibrosarcoma, I believe that the best thing to have done is what we did.

DR. CASTLEMAN: The boy was seen seven months after operation and was perfectly well, going to school and playing just like any other boy. His only complaint was tenderness in the upper portion of the operative field when it is washed, apparently due to the severed nerve roots close to the skin. Fourteen months after operation, however, the patient re-entered the hospital because of a recurrent nodule in the neck. The mass was located in the upper lateral portion of the operative field; it involved the lower lateral end of the sternal mastoid muscle and was adherent to the first rib. The nodule, which measured 7 by 3 by 3 cm., and the first rib were removed; on microscopical examination it was found to comprise neoplastic tissue identical with that of the original tumor.

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The Journal does not hold itself responsible for statements made by any contributor.

Communications should be addressed to the *New England Journal of Medicine*, 8 Fenway, Boston 15, Massachusetts.

## SHARE THE BLOOD!

There is an urgent, almost dramatic, need for blood donors to furnish plasma for our fighting men, and the medical profession, which should be such a potent factor in promoting this vital enterprise, is, in too many instances, handicapping it. Healthy civilians, both men and women, who need encouragement to give blood at safe and reasonable intervals are being deterred from it, frequently for insufficient reasons. We are not yet awake to our opportunity and our obligation, for the supply is inadequate and the need will soon become desperate as the time for invasion draws near.

A remarkable organization for the collection of human blood plasma has been developed. This was the result of a request made in May, 1941, by the surgeons general of the Army and Navy to the American Red Cross and the Division of Medical Sciences of the National Research Council. The function of the Red Cross has been to procure the donors, that of the National Research Council to supervise the professional services.[1] Through its various centers, the Red Cross met its quota of 4,000,000 pints of plasma in 1943; this year 5,300,000 pints will be required, and it must be noted that, owing to broken appointments, rejected volunteers and bloods, and certain irreducible technical losses, nearly 1250 persons must offer to give their blood for each 1000 units of dried plasma finally made available.

The blood collecting center in Boston, the only one in northern New England, is equipped to handle, during its six-day, sixty-eight-hour week, 800 donors daily, attaining, at times, a maximum speed of two bleedings per minute. The substation in Lynn and the three mobile units, operating at distances greater than twenty-five miles from Boston, are each equipped to bring in an additional 1000 pints weekly. The actual number of donors bled at the Boston center recently dropped to between 400 and 550 per day, and a large number of these are war workers and service men. The civilian population is not doing its share.

The safety and health of the donor are carefully protected. Each donor must be free from disqualifying disease and must have a normal temperature at the time of bleeding, as well as a hemoglobin level of 80 per cent or over by the Tallqvist method and a systolic blood pressure between 100 and 200. No donor is accepted oftener than five times in a year, with a minimum interval of eight weeks between donations. This interval seems conservative in view of the studies of Fowler and Barer,[2] who found that the average drop in hemoglobin of 2.3 gm. after the removal of 555 cc. of blood was restored on the average in approximately fifty days, the time being somewhat longer for women than for men, and that the rate of regeneration did not seem to be affected by repeated donations.

Psychic factors in certain persons may be more important deterrents to blood donating than physical ones. Let us all, however, when the oppor-

tunities come to give advice on the subject, weigh the evidence objectively, and encourage rather than discourage, unless we are certain that a person's health may suffer unduly from this act of mercy.


### References

1. Taylor, E. S. Procurement of blood for the armed services. *J. A. M. A.* **120**: 119, 1941.
2. Fowler, W. M., and Barer, A. P. Rate of hemoglobin regeneration in blood donors. *J. A. M. A.* **118**:421-431, 1942.


## TUBERCULOSIS AND THE WAR

The effect of war on tuberculosis death rates is generally considered to be inevitable and adverse. Heretofore it has always seemed to be so, although the slight increases in mortality observed in this country in 1917 and 1918 were more than compensated for by the subsequent accentuation of the downward curve. Anticipating that tuberculosis may again be "one of the camp followers of war," a committee of the American Trudeau Society* surveyed the personnel of the sanatoriums in this country and reported a distinct reduction during 1942. It is certain that this decrease in numbers, continuing on through 1943, is placing an ever-increasing burden on those who are left to operate the sanatoriums.

The war is also having an effect on the symbiotic relations between man and the tubercle bacillus. The armed services are rejecting, and thereby uncovering, many of the dangerous carriers among young men — those whose disease is symptomless but who nevertheless have open lesions from which they may freshly expose and widely spread the infection. From the millions of men examined at the induction stations, it is estimated that 25,000 had been diagnosed at the end of last year to have a disease that neither they nor their friends would have suspected under prewar conditions. And how are these patients, many of whom need sanatorium treatment, going to be accommodated by the currently restricted personnel of the sanatoriums?

Tuberculosis workers, who for some years past have been extending their case-finding activities, are thus suddenly having found for them more cases than they can conveniently care for. Morbidity rates should go up, but there will not be more actual sickness — it will merely be more completely recognized. The mortality rates need not go up at all, for most of the cases will do as well as they would have if they had not been recognized, and many of them do better. Furthermore, fewer contacts will result.

No evidence has yet been uncovered to indicate that the downward trend of the tuberculosis death rate has been seriously affected. Whether it will be adversely influenced by a prolonged continuation of the war is a purely relative matter, and is really an insignificant speculation in comparison to the total interests similarly involved. On the whole it seems that the war will accelerate the antituberculosis effort by forcing a decreased personnel to dedicate itself to an increased volume of labor: just as the training of doctors and engineers is being accelerated, just as the shipbuilders are launching an incredibly large number of ships, and just as the entire nation is bending itself to the task ahead. The *Journal* has sufficient confidence in all the forces involved to make a humble prediction that the war years will not show an increase in the mortality of tuberculosis in the United States. This statement is not a mere prophecy — it is an expression of confidence in the ability, ingenuity and steadfast qualities of those who specialize in the care and the cure of tuberculosis.

**Personal Problems of Sanatoria Resulting from War Conditions.* Report of a study made by the Committee on Sanatorium Standards, American Trudeau Society. 39 pp. New York: National Tuberculosis Association, 1943.

## MEDICAL EPONYM

### Rumpel-Leede Sign

Theodor Rumpel (1862–1923), director of the Barmbecker Krankenhaus in Hamburg and chief physician of the Second Medical Service of the Allgemeines Krankenhaus, presented "Photographien von Scharlachkranken mit multiplen Hautblutungen [Photographs of Scarlet-Fever Patients with Multiple Skin Hemorrhages]" at a meeting of the Aerztlicher Verein in Hamburg on June 13, 1909. A report appears in the *Deutsche medizinische Wochenschrift* (**35**[2]:2297, 1909). A portion of the translation follows:

> These hemorrhages, which also occur spontaneously on the forearm and in the bend of the elbow, in the areas where the exanthem is most marked, may be induced by mechanical stimuli, particularly by the application of a Bier's compression cuff to the upper arm, and are then of value in the differential diagnosis of scarlet fever.

Carl S. Leede (b. 1882), then assistant to Professor Rumpel and later a practitioner of internal medicine in Seattle, Washington, described "Hautblutungen durch Stauung hervorgerufen als diagnostisches Hilfsmittel beim Scharlach [Skin Hemorrhages Elicited by Congestion as a Diagnostic Aid in Scarlet Fever]" in the *Münchener medizinische Wochenschrift* (58[1]:293-295, 1911). A portion of the translation follows:

> At the request of [my] chief, Dr. Rumpel, who directed attention to the differential diagnostic significance of the phenomenon at the meeting of the medical society June 13, 1909, every case of scarlet fever was systematically subject to congestion by means of a rubber cuff applied to the upper arm so that the veins stood out distinctly while the pulse remained palpable.
>
> Hereupon, almost without exception, among cases of scarlet fever (several hundred were examined) more or less marked skin hemorrhages appeared. . . .
>
> In my experience a *negative* result of the congestion test may be used as an almost certain criterion against scarlet fever, whereas a *positive* result may be evaluated only together with other symptoms.
>
> We perform the congestion test at the present time as follows:
>
> A broad rubber cuff is placed about the upper arm above the elbow so that the veins stand out distinctly; the hand becomes blue, but the pulse remains palpable. After ten to fifteen minutes we loosen the cuff and examine the tender skin of the fold of the elbow, at the same time making the skin anemic by means of stretching it, whereupon the petechiae stand out more distinctly as a dark spray.
>
> We call the congestion test positive even though we find only a moderate number of petechiae.

R. W. B.

## MASSACHUSETTS MEDICAL SOCIETY

### DEATHS

PERLEY — Roscoe D. Perley, M.D., of Melrose, died January 21. He was in his eighty-first year.

Dr. Perley received his degree from Harvard Medical School in 1896. He was a former member of the staffs of the Massachusetts General Hospital and the Boston Lying-in Hospital and was on the surgical staff of the Melrose Hospital for forty years. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow, a son and a daughter survive.

RICH — Herbert L. Rich, M.D., of Attleboro, died January 23. He was in his seventy-ninth year.

Dr. Rich received his degree from Tufts College Medical School in 1898. He was a member of the Massachusetts Medical Society and the American Medical Association.

His widow and a brother survive.

## MASSACHUSETTS DEPARTMENT OF PUBLIC HEALTH

### CHANCROID, GRANULOMA INGUINALE AND LYMPHOGRANULOMA VENEREUM MADE REPORTABLE

As provided by the General Laws, Chapter 111, Section 6, the Department of Public Health has defined and made reportable the diseases *chancroid*, *granuloma inguinale* and *lymphogranuloma venereum*. Physicians in Massachusetts are required to report these diseases directly to the Department of Public Health under the same conditions, rules and regulations as now pertain to the reporting of syphilis and gonorrhea; and further, to use the same report form that is now provided by the department to report syphilis and gonorrhea for the purpose of reporting these three other diseases. For the present, it is suggested that the physician write on the report form the name of the disease he is reporting and strike out the words, "syphilis" and "gonorrhea."

Prepared spreads of material collected from the undermined edges of the suspected chancroidal ulceration or, still better, from the aspirated pus of the bubo may be submitted by the physician to the Bacteriological Laboratory, State House, Boston, for diagnosis. A spread of macerated tissue from the active edge of a lesion thought to be granuloma inguinale may also be sent to the laboratory. Antigen for skin testing for lymphogranuloma venereum will soon be available from the Antitoxin and Vaccine Laboratory for free distribution to private physicians. Literature dealing in detail with the management of these diseases by the physician may be obtained from the Department of Public Health.

### CONSULTATION CLINICS FOR CRIPPLED CHILDREN IN MASSACHUSETTS

| Clinic | Date | Clinic Consultant |
|---|---|---|
| Haverhill | February 2 | William T. Green |
| Lowell | February 4 | Albert H. Brewster |
| Salem | February 7 | Paul W. Hugenberger |
| Brockton | February 10 | George W. VanGorder |
| Springfield | February 16 | Garry deN. Hough, Jr. |
| Worcester | February 18 | John W. O'Meara |
| Pittsfield | February 21 | Frank A. Slowick |
| Fall River | February 28 | Eugene A. McCarthy |
| Hyannis | February 29 | Paul L. Norton |

## MISCELLANY

### THE ELLA SACHS PLOTZ FOUNDATION

During the twentieth year of the Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation, eighteen applications for grants were received by the trustees, thirteen of which came from the United States, the other five coming from five different countries in Europe, Asia, North and South America. In the twenty years of its existence the Foundation has made four hundred and eighty-one grants which have been distributed to scientists throughout the world.

In their first statement regarding the purposes for which the fund would be used, the trustees expressed themselves as follows:

1. For the present, researches will be favored that are directed toward the solution of problems in medicine and surgery or in branches of science bearing on medicine and surgery.
2. As a rule, preference will be given to researches on a single problem or on closely allied problems; it is hoped that investigators in this and in other countries may be found, whose work on similar or related problems may be assisted so that more rapid progress may be made possible.
3. Grants may be used for the purchase of apparatus and supplies that are needed for special investigations, and for the payment of unusual expenses incident to such investigations, including technical assistance, but not for providing apparatus or materials which are, ordinarily, a part of laboratory equipment. Stipends for the support of investigators will be granted only under exceptional circumstances.

In the past few years the policy outlined in paragraph 2 has been neglected. Grants will be given in the sciences closely related to medicine without reference to special fields. The maximum size of grants will usually be less than $500.

Applications for grants to be held during the year 1944-1945 must be in the hands of the committee before April, 1944. There are no formal application blanks but letters asking for aid must state definitely the qualifications of the investigator, an accurate description of the research, the size of the grant requested and the specific use of the money to be expended. In their requests for aid applicants should state whether or not they have approached other foundations for financial assistance. It is highly desirable to include letters of recommendation from the directors of the departments in which the work is to be done. Only applications complying with the above conditions will be considered.

Applications should be sent to Dr. Joseph C. Aub, Massachusetts General Hospital, Fruit Street, Boston.

## CORRESPONDENCE

### APPEAL FOR BOOKS

*To the Editor:* This is a personal appeal. We need your help. The National Victory Book Campaign terminated on December 31, 1943. An unfortunate impression has become current, that the campaign was wound up because it had collected all the books needed. Nothing could be further from the facts. — The men in our armed forces and in the Merchant Marine need books *desperately.*

The Massachusetts Victory Book Committee has been formed to carry on in Massachusetts from where the National Victory Book Campaign left off. The Massachusetts Committee has set its minimum goal at 250,000 volumes. All types of books, in good condition, are welcome. Biographies, travel, science, religion, but especially good fiction — mysteries, westerns and comics — are in demand. Visualize how men on long sea voyages, on dreary coast patrols, in lonely outposts and in the remote parts of the world yearn for something to read.

The Massachusetts Victory Book Committee needs your help. It asks you personally and in your official capacity to enlist the wholehearted efforts of your readers.

Every book donated will reach the armed forces where it is most wanted. Distribution will be handled by Special Service officers of the Army and the Welfare officers of the Navy. The merchant-marine and the Red Cross military hospitals will also receive their share.

You are familiar with the slogan "Get the Vote Out." This committee's slogan is "Get the Books Out." It is a big job, but it must be done.

Books should be left at local public libraries or at the nearest Information Center of the Massachusetts Committee on Public Safety. This committee will do the rest.

JOHN HEARD, *Secretary*
Massachusetts Victory Book Committee

13 Commonwealth Avenue
Boston 16

## NOTICES

### UROLOGY AWARD

The American Urological Association offers an annual award "not to exceed $500" for an essay (or essays) on the result of some specific clinical or laboratory research in urology. The amount of the prize is based on the merits of the work presented, and if the members of the Committee on Scientific Research deem none of the offerings worthy, no award will be made. Competitors shall be limited to residents in urology in recognized hospitals and to urologists who have been in such specific practice for not more than five years. All interested should write the secretary for full particulars.

The selected essay (or essays) will appear on the program of the forthcoming meeting of the American Urological Association, June 19–22, 1944, Hotel Jefferson, St. Louis, Missouri.

Essays must be in the hands of the secretary, Dr. Thomas D. Moore, 899 Madison Avenue, Memphis, Tennessee, on or before March 15, 1944.

### NEW ENGLAND HOSPITAL FOR WOMEN AND CHILDREN

The monthly clinical conference and meeting of the staff of the New England Hospital for Women and Children will be held on Thursday, February 3, in the classroom of the Nurses' Residence, at 7:15 p.m. Dr. Francis L. Weille will speak on the subject "Treatment of Sinusitis." Dr. Elizabeth DeBlois will be chairman.

### JOSEPH H. PRATT DIAGNOSTIC HOSPITAL

Bennet Street, Boston

Lecture Hall, 9–10 a.m.

MEDICAL CONFERENCE PROGRAM

Wednesday, February 2 — To be announced. Dr. John D. Adams.

Friday, February 4 — Clinical Importance of Cold Hemagglutinins. Dr. Cutting B. Favour.

Wednesday, February 9 — The Diagnosis of Pancreatic Disease. Dr. Joseph H. Pratt.

Friday, February 11 — Clinicopathological conference. Dr. Chester S. Keefer and Dr. Harold E. McMahon.

Wednesday, February 16 — Constipation. Dr. Edwin T. Whitney.

Friday, February 18 — Some Postwar Aspects of Malaria. Dr. William C. McCarthy.

Wednesday, February 23 — Mechanisms Predisposing to Pneumonia. Dr. Dwight O'Hara.

Friday, February 25 — Visualization of the Biliary Tract. Dr. Charles G. Mixter.

On Tuesday and Thursday mornings Dr. S. J. Thannhauser will give medical clinics on hospital cases.

### WASHINGTONIAN HOSPITAL

The second lecture in a series on various aspects of alcoholism, arranged by the Washingtonian Hospital and being given under its auspices and that of the Committee on Alcoholism of the Boston Council of Social Agencies, will be held at Zero Marlborough Street, Boston, at 7:30 on Friday evening, February 11. The speaker will be Dwight Anderson, LL.B., director, Public Relations, Medical Society of the State of New York, and his topic, "Alcohol and Public Opinion."

### NEW ENGLAND DERMATOLOGICAL SOCIETY

The regular meeting of the New England Dermatological Society will be held in the Skin Out Patient Department of the Massachusetts General Hospital on Wednesday, February 9, at 2 p.m.

### SOCIETY MEETINGS AND CONFERENCES

CALENDAR OF BOSTON DISTRICT FOR THE WEEK BEGINNING THURSDAY, FEBRUARY 3

THURSDAY, FEBRUARY 3

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser, Joseph H. Pratt Diagnostic Hospital.

7:15 p.m. Treatment of Sinusitis. Dr. Francis L. Weille. New England Hospital for Women and Children.

FRIDAY, FEBRUARY 4

*9:00–10:00 a.m. Clinical Importance of Cold Hemagglutinins. Dr. Cutting B. Favour. Joseph H. Pratt Diagnostic Hospital.

SATURDAY, FEBRUARY 5

*10:00–11:30 a.m. Medical staff rounds. Peter Bent Brigham Hospital.

(*Continued on page xiii*)

NOTICES *(Continued from page 124)*

MONDAY, FEBRUARY 7

*12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital.

TUESDAY, FEBRUARY 8

*9:00–10:00 a.m. Medical clinic. Dr. S. J. Thannhauser. Joseph H. Pratt Diagnostic Hospital.

*12:15–1:15 p.m. Clinicoroentgenological conference. Peter Bent Brigham Hospital.

2:00–4:00 p.m. Myasthenia gravis clinic. Out Patient Department, Massachusetts General Hospital.

WEDNESDAY, FEBRUARY 9

*9:00–10:00 a.m. The Diagnosis of Pancreatic Disease. Dr. Joseph H. Pratt. Joseph H. Pratt Diagnostic Hospital.

*12:00 m. Clinicopathological conference. Children's Hospital.

2:00 p.m. New England Dermatological Society. Massachusetts General Hospital. Skin Out Patient Department.

*Open to the medical profession.

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FEBRUARY 2–25. Joseph H. Pratt Diagnostic Hospital. Medical conference program. Page 124.

FEBRUARY 10. Pentucket Association of Physicians. 8:30 p.m. Haverhill.

FEBRUARY 11. Washingtonian Hospital. Various aspects of alcoholism. Page 124.

FEBRUARY 12. American Board of Obstetrics and Gynecology. Page 30, issue of January 5.

FEBRUARY 13. National Conference on Medical Service. Page x, issue of January 6.

MAY 23 and 24. Massachusetts Medical Society. Annual meeting, Hotel Statler, Boston.

JUNE 12–16. American Medical Association. Annual meeting, Chicago. Page 798, issue of November 18.

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DISTRICT MEDICAL SOCIETY

WORCESTER

FEBRUARY 9. Worcester State Hospital, Worcester.
MARCH 8. St. Vincent Hospital, Worcester.
APRIL 12. Hahnemann Hospital, Worcester.
MAY 10. Annual meeting.


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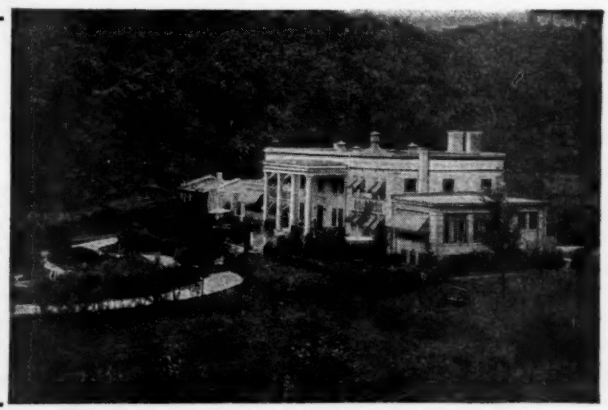

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